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## CONGENITAL CYSTIC DISEASE OF THE LUNG IN INFANTS AND IN CHILDREN

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AND

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BALTIMORE

**D**ESPITE a rapidly growing literature on cysts of the lung, there still exists a considerable disparity of opinion with reference to their genesis, diagnosis and mode of treatment. A recent monograph<sup>1</sup> stated:

Congenital cystic disease: Anatomic studies indicate that this is an extremely rare condition. It has not been found at necropsy at The Babies Hospital during a period of fifty years. Schenck quotes Lederer as having failed to find a single instance of congenital cystic disease in five thousand necropsies. It is now evident that many cases which have suggested congenital cysts roentgenographically were probably examples of acquired emphysematous cavities caused by check-valvular bronchial obstruction.

The present cases of cystic disease of the lung in infants and children exemplify most types of cystic disease of the lung seen and present a fair sample of the types of accompanying anatomic anomalies (fig. 1). Ten of the 12 patients have been seen consecutively in the past five years, 8 of them within the past year.

The occurrence of the disease in newborn infants (Flemming Möller<sup>2</sup>) establishes it as congenital. The embryologic mechanism and the time of formation of the defect have not been established. The frequent association of anomalous lobar segments—as in cases 7 and 8 and as reported by Harrington,<sup>3</sup> Flemming Möller<sup>2</sup> and others—suggests a gross developmental disturbance, as does the frequent occurrence of anomalous systemic arteries supplying the lung (cases 8 and 9 and reports by Douglass,<sup>4</sup> Haight<sup>5</sup> and others). The occurrence in

From the Department of Surgery of The Johns Hopkins Medical School and Hospital and the Harriet Lane Home.

1. Caffee, J.: *Pediatric X-Ray Diagnosis*, Chicago, The Year Book Publishers, Inc., 1945, p. 234.

2. Flemming Möller, P.: *Congenital Thoracic Cysts and Lung Deformities in the Roentgen Picture*, *Acta. radiol.* 9:460, 1928.

3. Harrington, S. W.: *Surgical Treatment of Intrathoracic Tumors*, *Arch. Surg.* 19:1679 (Dec.) 1929.

4. Douglass, R., in discussion on Brown and Brock.<sup>13</sup>

5. Haight, C., in discussion on Brown and Brock.<sup>13</sup>



the same lobes of adenomatous growth of the mucous glands, as seen in case 6 (fig. 14*A*), has been reported by others. These various anomalies are usually not accompanied with major defects in other organs. Supplementary lobes and anomalous vessels are found without cysts of the lung and cannot in themselves be causative factors. Lobes supplied by anomalous arteries may also have normal pulmonary arteries. It is of interest that in a series of over 400 cases of pulmonic stenosis observed at the Johns Hopkins Hospital, in some of which the pulmonary arteries to one or both lungs were absent, only 1 patient has been found to have what appears to be a cyst of the lung.

Abnormally situated vessels present a hazard during the course of operation which may be minimized by an awareness of their possible

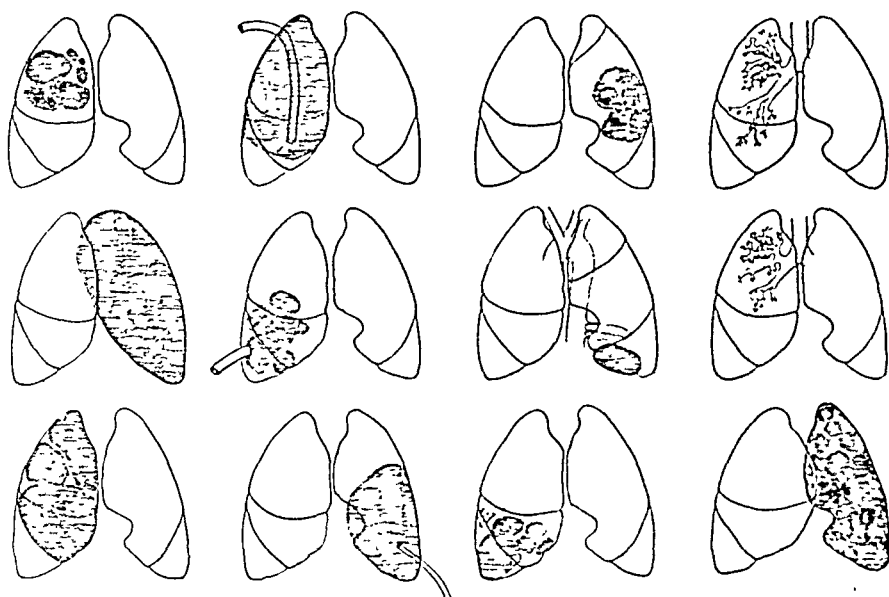


Fig. 1—Distribution and character of the lesions found in the 12 patients reported on. First column, cases 1, 2 and 3; second column, cases 4, 5 and 6; third column, cases 7, 8 and 9; fourth column, cases 10, 11 and 12. The patients in cases 1, 2 and 3 were infants; those in 2 and 6 had a check valve mechanism; those in 4, 5 and 6 had been drained for empyema, and were admitted with tubes in place; those in 7 and 8 had trilobed left lungs; those in 8 and 9 had anomalous systemic arteries supplying the affected lobes; those in 10 and 11 had a cystic bronchiectasis of the right upper lobe, and the patient in case 12 had a left lung honeycombed with cysts.

presence. McCotter in 1910<sup>6</sup> analyzed 9 cases of anomalous pulmonary arterial blood supply gathered from the literature of the preceding century. In 5 instances these arteries supplied accessory lower lobes of the infracardiac type, four of which were situated on the left and the fifth on the right. These vessels all arose from the aorta between

6. McCotter, R. E.: On the Occurrence of Pulmonary Arteries Arising from the Aorta, *Anat. Rec.* 4:291, 1910.

the levels of the seventh and tenth thoracic vertebrae. In the remaining 4 cases the anomalous vessels were not associated with accessory lobes but represented an abnormal blood supply to lobes which seemed otherwise normal. In 3 of these the vessels arose from the thoracic aorta; two supplied the lower lobe on the left, and the third supplied the lower lobe on the right. In the fourth the vessel arose from the abdominal aorta, and after passing through the esophageal hiatus in the diaphragm it branched to supply the lower lobes of both right and left lungs.

Batts<sup>7</sup> described a patient in whom a large artery arising from the celiac plexus passed through the diaphragm to supply the lower lobe of the left lung. In Harris'<sup>8</sup> case an operative fatality resulted from hemorrhage due to the inadvertent cutting of a large artery arising from the thoracic aorta 2 cm. above the diaphragm and entering the lower lobe of the left lung posteriorly at the level of the free margin of the pulmonary ligament.

In discussing Moersch and Clagett's report on pulmonary cysts, Head<sup>9</sup> described a cystic accessory pulmonary lobe which had a bronchial system continuous with that of the normal lower lobe of the left lung but which derived its main blood supply from the thoracic aorta. In further discussion Butler<sup>10</sup> commented on finding anomalous systemic arteries to the lung in at least four operations for congenital cystic disease, with fatal hemorrhage from such a vessel in 1 instance.

As Harris and Ivor<sup>8</sup> have pointed out, the anomalous pulmonary arteries fall into two groups, both consisting of persistent enlargement of the embryonic capillary plexuses. In the first group the connections are between the pulmonary artery and the subclavian, the superior intercostal or the ventral splanchnic branches of the aorta. In the second group the connections are between the pulmonary artery and the celiac axis.

Various authors have commented on the association between accessory pulmonary lobar segments and cystic disease. Schenck<sup>11</sup> in his analysis of the 232 cases of cystic disease reported up to 1936 pointed out that 38 of the patients were found at autopsy to have other malformations in addition to the cystic disease of the lung. The most

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7. Batts, M.: A Pulmonary Artery Arising from the Aorta, *J. Thoracic Surg.* 8:565, 1939.

8. Harris, H. A., and Ivor, L.: Anomalies of the Lung with Special Reference to Danger of Abnormal Vessels in Lobectomy, *J. Thoracic Surg.* 9:666, 1940.

9. Head, J., in discussion on Moersch.<sup>14</sup>

10. Butler, E. F., in discussion on Moersch.<sup>14</sup>

11. Schenck, S. G.: Congenital Cystic Disease of the Lungs, *Am. J. Roentgenol.* 35:608, 1936.

frequent of these congenital abnormalities was the presence of an accessory pulmonary lobe harboring the cystic areas. This was found in 17 patients.

The derivation of these cysts from malformed bronchi is clearly indicated by the unquestionably bronchial character of the epithelium (figs. 4 *B* and 12 *B*) and the elastic tissue, smooth muscle or cartilage in the walls. Again, the cysts are almost invariably at the periphery of the lung (unless the lung is entirely honeycombed, as in case 12, fig. 25), which suggests that it is the small peripheral bronchi which have failed to establish communication with the air spaces.

#### CLINICAL CHARACTERISTICS

The clinical behavior of cysts of the lung can be predicted from their structure and the known mechanism of the symptomatology of pulmonary disease. The division of congenital cysts into "air cysts" and "fluid cysts" is probably arbitrary although it suggests at once the salient characteristic of the given cyst or cysts. In every one of our patients communication of the cyst or cysts with the bronchial tree was demonstrated in one or several ways. In cases 6, 7, 10, 11 and 12 bronchograms showed lipiodol® (iodized poppyseed oil 40 per cent) in the cysts. At operation in cases 2 and 6 a check valve communication with a large bronchus was demonstrated. The patients in cases 4, 5 and 6, who were treated elsewhere for what was thought to be empyema, had frank bronchopleural fistulas, intermittent in cases 4 and 5 and constant in case 6. In case 8 anthracotic pigment in the cyst and copious purulent sputum proved the bronchial communication. In the others, cases 1, 3 and 9, air in the cysts was visible in the roentgenograms. Demonstration of a bronchial communication in the gross specimen has been notoriously difficult even when bronchography has proved such communication to exist. The presence in the lung of a cavity lined by secreting epithelium and communicating with the bronchial tree gives rise to cough, expectoration, infection of the cyst and a train of consequences similar to those seen in cases of bronchiectasis and of pulmonary abscess. The infection originating in these cysts may give rise to a secondary bronchiectasis as a result of compression of neighboring pulmonary tissue and overflow of purulent secretions. The mucous membrane lining these cysts is usually intact, and, as might be expected, none of the patients had hemoptysis or metastatic abscesses.

In only 1 case (case 6) was the cyst found on a routine roentgenogram of an asymptomatic child. This child subsequently had frequent attacks of "bronchopneumonia" and finally had a cyst drained six years before we saw him. Seven of the others had a chronic cough,

the age at onset being from 3 weeks to 5 years. In 3 who were previously asymptomatic evidence of acute pulmonary infection developed at the ages of 8, 9 and 12 years. Six of the patients had repeated bouts of pulmonary infection severe enough to be called pneumonia. Dyspnea, constant or in episodes, was observed in all patients. Severe cyanosis was seen only in the patient in case 10, who had associated bronchiectasis of the lower lobes.

Inevitability of infection in cysts of the lungs is the strongest reason for early, prophylactic operation. The advisability of operation is frequently questioned in children with apparently asymptomatic cysts, as in the patient in case 1, who, at the age of 3 months, had had a cough for three weeks and was found to have cysts in the right upper pulmonary field. He was well nourished, afebrile and vigorous. Operation was advised and performed to forestall the inevitable infection. Aspiration of the cysts at operation showed yellow fluid which yielded a pure culture of staphylococci. The microscopic sections (fig. 4) showed extensive inflammation of the lining of the cyst despite the age of the patient and absence of symptoms. In only 1 patient (case 2, fig. 7) was there absence of considerable inflammatory changes in the cyst. The single death in the series, in case 3, was due to pneumonia supervening in a child with heavily infected cysts who had unfortunately been sent home "to be built up" (fig. 8).

Rupture of cysts, with resultant pneumothorax or empyema or both, has been reported but was not seen in this series. Similarly, others have reported hemoptysis in patients with cyst of the lung. One would expect hemoptysis only if the infection has been severe enough to destroy the cyst lining or if there is associated bronchiectasis.

The literature is replete with reports of patients with cystic disease of the lung erroneously treated for empyema (Maier & Haight<sup>12</sup>), the true source of the infected fluid being discovered subsequently. The patients in cases 4, 5 and 6 (figs. 9 to 14) all came to us with a drainage tube in place. It has frequently been remarked that long-continued drainage of cysts of the lungs does not affect their size—which is borne out by the roentgenograms of these patients seven months, five years and six years, respectively, after drainage was instituted.

One occasionally sees tension cysts, the so-called giant cysts or gas cysts, with symptoms due chiefly to pressure. Cases 2 and 6 exemplify the mechanism in such instances. In the first, involving a year old infant, the entire left side of the chest was filled with a huge air-containing cyst (fig. 5) which crossed the midline to the right. At operation

12. Maier, H. C., and Haight, C.: Large Infected Solitary Pulmonary Cysts Simulating Empyema, *J. Thoracic Surg.* 9:471, 1940.

the cyst was so large (fig. 6) that it was aspirated with a needle and emptied of air to facilitate the operation. Almost at once it refilled with air and became as large and tense as ever. It seemed clear that there was a one way valve which permitted ingress of air until the tension within the cyst was sufficient to occlude the bronchus, equilibrium being established at a point within the range of tolerance of the patient. To complete the operation it was necessary to leave a large needle penetrating the cyst cavity, permitting release of the entrapped air. In the second instance (case 6) there was a cutaneous fistula of six years' duration which had given the patient no difficulty except for the slight annoyance incident to a cutaneous bronchial fistula. When, at operation, this sinus tract was dissected out within the chest and clamped off, the cyst began to balloon out tensely. As soon as the clamp was released the cyst returned to its former size. Again there was a one way valve, which in this case had been compensated for by a permanent external fistula.

While the general systemic response has varied with the extent of the pulmonary tissue involved and the degree of infection in it, clubbing of the fingers appears to be singularly infrequent, occurring in only 2 of our cases, 10 and 12.

#### PATHOLOGIC CHARACTERISTICS

The ultimate criterion for the diagnosis of congenital cystic disease of the lung in most cases is the gross and microscopic pathologic picture. It is remarkable how little the characteristics of congenital cysts are altered by prolonged and severe infection. In our present series we recognize three types of cysts on gross pathologic grounds and only two on microscopic grounds. Cases 3, 9 and 12 represent lobes or lungs honeycombed by cysts, most graphically seen in case 12, in which the entire left lung was replaced by innumerable cysts of varying size (fig. 25). In case 9 the lower lobe of the right lung (fig. 19) and in case 3 the upper lobe (fig. 8) were similarly affected. It occasionally occurs that all lobes of both lungs are so diseased, and in July 1945 one of us (M. M. R.) saw a patient in whom this occurred in the wards of the Brompton Hospital in London on the service of A. Tudor-Edwards—a 6 year old girl with both lungs presenting the appearance of the left lung in our case 12. The patients in cases 1, 2, 4, 5, 6 and 8 had cysts of one lobe and the patient in case 7 had cysts of two lobes, the cysts being either unilocular or else a few large cysts coalescing to form what was essentially a unilocular cyst with out-pouchings. Microscopically the cysts in both these types are indistinguishable. Characteristically the lining is of tall, columnar, typical bronchial epithelium. Cilia can be plainly seen in the photomicrographs in cases 1, 5 and 8, despite the fact that the patient in case 5

had had a rib resection and had worn a drainage tube for five years and the patient in case 8 had a cyst filled with pus and had had the clinical symptoms of a pulmonary abscess. Case 2 fits most closely the group of so-called air cysts, and here the epithelium is low cuboidal. In the cysts in case 3 gross infection has left only granulation tissue, with occasional epithelial remnants which are low cuboidal. The structure of the cyst walls varies. Some photomicrographs show well defined layers of smooth muscle and elastic tissue; in others there is only a nondescript, laminated fibrous wall. Many of the cysts have bronchial glands in their wall or beneath. Figure 14 *A* from case 6 shows an adenomatous proliferation of mucous glands deriving from the cyst epithelium, and figure 14 *B* from the same case shows a similar proliferation of mucous glands in the parenchyma of the lung at a distance from the cyst wall. The lungs have usually been scarred and compressed near the cysts. It is remarkable that in the gross specimen the lining of the cyst usually seems white, shiny and smooth regardless of the amount of inflammation which may appear. The trabeculation of the walls of many of the cysts produces an appearance of involved infolding in the microscopic section.

Our cases 10 and 11 present the third type of cyst, based on the gross appearance. These are perhaps the last cases left in the group of "congenital bronchiectasis," a once popular diagnosis. The history of the patients as given here, the peculiar site of the disease—the upper lobe of the right lung—and the unusual arrangement of the uniform sacculations along the bronchial tree all suggest a congenital malformation of the bronchi. On the basis of the microscopic picture it is not possible to make a categoric differentiation from acquired bronchiectasis. However, the photomicrographs of case 10 show a large bronchial structure with well preserved mucosa, a thick fibrous wall, astonishingly little evidence of infection and no cartilage at all. Beneath the wall of the large cavity is a cross section of what appears to be a smaller cyst. In case 11 also the photomicrographs show a curious lack of inflammation. There is dense scarring of the lung, with numerous large bronchus-like tubes. The epithelium is well preserved. In some areas are many small, round, epithelium-lined spaces, probably regenerated alveoli but possibly small cystic spaces. The preponderant evidence in these 2 cases is in favor of something other than ordinary bronchiectasis, and we feel justified in suggesting that they may represent instances of congenital diffuse saccular dilatation of the bronchi in the upper lobe of the right lung, a special variety of cystic disease. The concept of "congenital bronchiectasis" has deservedly lost its popularity as a consequence of greater familiarity with pulmonary disease in children. Bronchiectasis is in large part a disease of childhood, at least one originating during childhood, but congenital dilatation of the

bronchi is an uncommon condition rather than one frequently met, as used to be thought. The picture presented by cases 10 and 11 has not been seen in a considerable number of children with bronchiectasis.

Dr. Richard H. Follis Jr., of the Department of Pathology, has reviewed the pathologic material with us.

#### DIAGNOSIS

The diagnosis is based largely on the roentgenographic appearance of the lesions and has usually been fairly obvious. It was in doubt only in case 8, in which a pulmonary abscess was considered to be present until, at operation, the finding of anomalous arteries and a trilobed left lung suggested the probability that this was a cyst of the lung. The photomicrographs (fig. 18 *B*) unquestionably show a cyst. In reviewing the records of the Harriet Lane Home, we were struck by the fact that whenever there was real difficulty in making a categoric diagnosis of cystic disease it was ultimately determined that some other condition obtained. In infants and children pulmonary abscesses and spontaneous pneumothoraces or pyopneumothoraces have given rise to the most diagnostic confusion. Abscesses usually have more surrounding inflammatory reaction in the pulmonary parenchyma, and there is an acute onset of symptoms following a respiratory infection. In children abscesses usually resolve but occasionally cause empyema. In spontaneous pneumothorax there is usually not the clearly outlined spherical air pocket seen in cystic disease. Obviously, if pneumothorax is a likely diagnostic possibility, operation should be deferred to permit time for the resorption of air to make the diagnosis clear. Occasionally this may take months. In children, bronchiectasis has not suggested cystic disease of the lung. Tuberculous cavities may be embarrassingly like cysts both in children and in adults. Eventually one will undoubtedly encounter a case of cystic disease with superimposed tuberculosis, but it would appear sound to reckon as tuberculous any cystic cavity in a patient whose sputum contains the organisms of the disease.

#### TREATMENT

The treatment of cystic disease of the lung is now on a sound basis. An ill drained cyst communicating with a bronchus presents the constant hazard of infection. The problem is a mechanical one. Drugs, bronchoscopic aspiration and other forms of treatment offer only palliation. Drainage of the cyst, if it is unilocular and drainage is dependent as in case 6, produces relief from all symptoms and establishes a broncho-pleural fistula. It has been recommended (Brown and Brock<sup>13</sup>) that

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13. Brown, H. L., and Brock, W.: A Method of Treatment of Large Pulmonary Air Cysts (Balloon Cysts) by an Endocutaneous Flap, *J. Thoracic Surg.* **11**:617, 1942.

permanent fistulas be created by suturing the skin into the cysts. Such methods are still palliative and may not be successful. The proper treatment seems to be extirpation of the cyst or cysts. Usually this requires a lobectomy, but it may be possible to remove the cyst wall without any pulmonary parenchyma. Cauterization of the cyst wall and attempted closure of the bronchial fistulas are, again, attempts at less direct relief of the patient's difficulty. It has been suggested that infected cysts be first drained and then resected (Maier<sup>12</sup>). We feel that this only complicates the ultimate operation. Preoperative therapy should consist in postural drainage, repeated bronchoscopic aspiration and the administration of penicillin aerosol and penicillin intramuscularly. Ten of the 12 patients were subjected to a lobectomy and 1 to a pneumonectomy, and all 11 recovered without the occurrence of empyema or fistula, although several patients previously had been febrile and had thick pus in their cysts. One patient (case 3) was sent home at the age of 8 months for improvement of her condition before operation and died within three weeks of an acute recrudescence of her pulmonary infection.

The time for operation is the time at which the diagnosis is made. In the absence of complicating factors, children with congenital cystic disease of the lung should be operated on whether the cysts are symptomatic or not. Infection is an almost invariable occurrence if the cysts are not removed. Reports by Moersch<sup>14</sup> and Graham<sup>15</sup> suggest that carcinoma may develop within a cyst. Infants stand pulmonary surgery remarkably well, and the procedures are actually much easier than in adults. The patient in case 1 was only 3 months old, and Gross<sup>16</sup> has reported a pneumonectomy in a 3 week old infant.<sup>16a</sup> We feel that in a case of uncomplicated unilateral cystic disease one is not justified in postponing operation "until the child grows larger." In operating it is important to remember the frequent occurrence of anomalies of lobes and vessels. In our case 7, with three lobes on the left, the "upper lobe" (actually the apical and subapical segments of the upper lobe) was a minute segment of pulmonary tissue, completely collapsed against the inner corner of the dome of the pleura. This lobe was not removed and has since filled the entire left pleural cavity (fig. 15 D). The anomalous systemic vessels in cases 8 and 9 were readily seen and gave rise to no technical difficulty.

14. Moersch, H. J., and Clagett, O. T.: *Pulmonary Cysts*, J. Thoracic Surg. **16**:179, 1947.

15. Graham, E., in discussion on Moersch.<sup>14</sup>

16. Gross, R.: *Congenital Cystic Lung: Successful Pneumonectomy in a Three Weeks Old Baby*, Ann. Surg. **123**:229, 1946.

16a. Since this paper was submitted, Burnett and Caswell have reported the successful outcome of lobectomy on an even younger patient for severe respiratory distress (Burnett, W. E., and Caswell, H. T.: *Lobectomy for Pulmonary Cysts in a Fifteen-Day Old Infant with Recovery*, Surgery **23**:84-91, 1948).



## REPORT OF CASES

CASE 1.—E. M., a white male infant, was 13 weeks of age at operation. He had a hacking cough for three weeks before his admission to the hospital. A roentgenogram taken to investigate the cough showed a mass in the right upper region of the chest. Two roentgen treatments produced no change, and he was referred to the hospital.

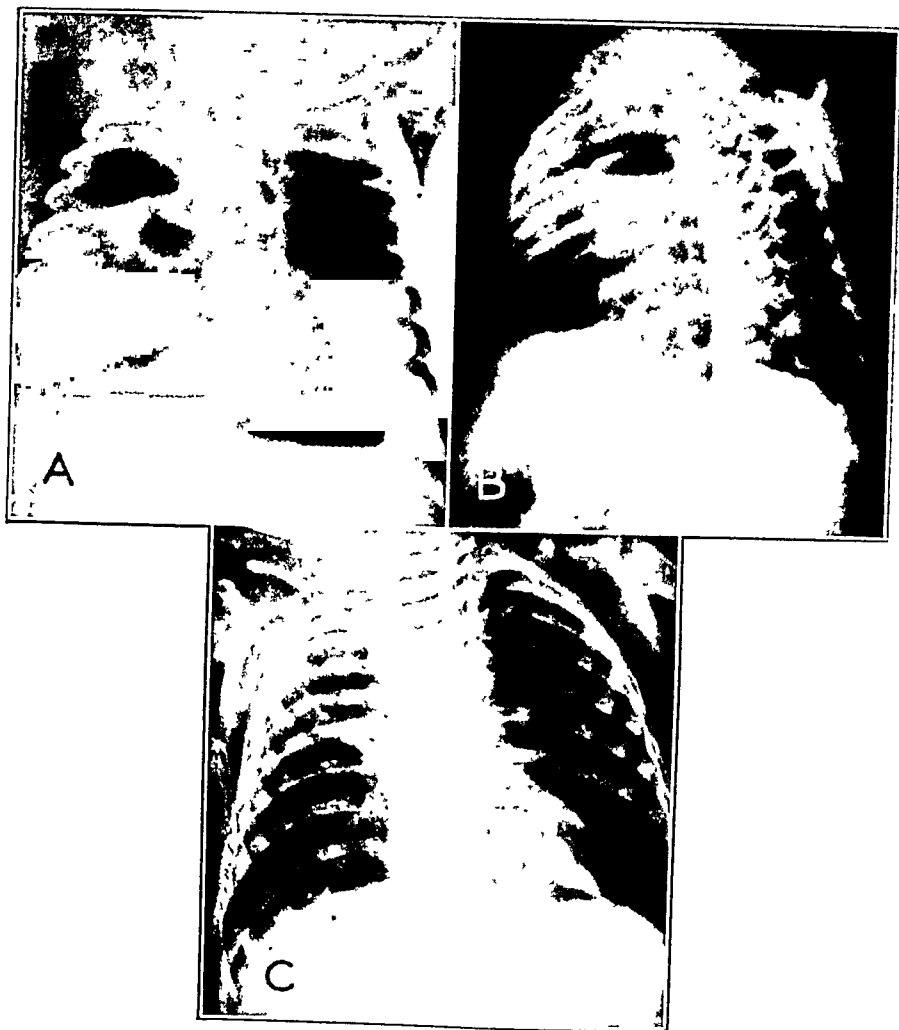


Fig. 2 (case 1).—*A* and *B*, roentgenograms, anteroposterior and oblique views, showing cysts in right upper pulmonary field. *C*, postoperative roentgenogram showing residual pleural thickening.

Physical examination showed a vigorous, healthy-looking infant. There was no asymmetry of the chest. The percussion note was impaired over the right upper region of the chest anteriorly and posteriorly, and in this area there were no breath sounds. Roentgenograms showed what was interpreted as a cystic tumor of the upper lobe of the right lung, thought to be multilocular (fig. 2). Air was seen in several round cystic spaces in a diffusely opaque upper lobe. There was a good deal of discussion on the advisability of operation since the child

# RAVITCH-HARDY—CONGENITAL CYSTIC DISEASE OF LUNG 11

seemed so well and had no fever and only a slight cough. Operation was advised because of the strong probability that infection would supervene in what were thought to be congenital cysts.

*Operation* (March 2, 1943, Dr. Blalock; upper and middle lobes of right lung excised).—The upper lobe alone seemed involved, but it was fused to the middle lobe, which was removed with it. One of the cysts tore and leaked a little yellow fluid, which on culture yielded *Staphylococcus albus*. After operation the child's course was uneventful except for slow reexpansion of the lung.

*Pathologic Report*.—The specimen (fig. 3) consists of the upper and middle lobes of the right lung of an infant. The upper lobe is largely occupied by a multilocular cyst 5.5 cm. in greatest diameter. The cyst is seen to be filled with pus. The lining, for the most part well preserved, consists of the upper and middle bronchial epithelium (fig. 4). There are a few mucous glands in the wall of the cyst and a narrow layer of smooth muscle between the basement membrane and the fibrous wall of the cyst. The cyst wall shows acute inflammation (fig. 4A), and the underlying lung shows inflammation and organization, with obliteration of

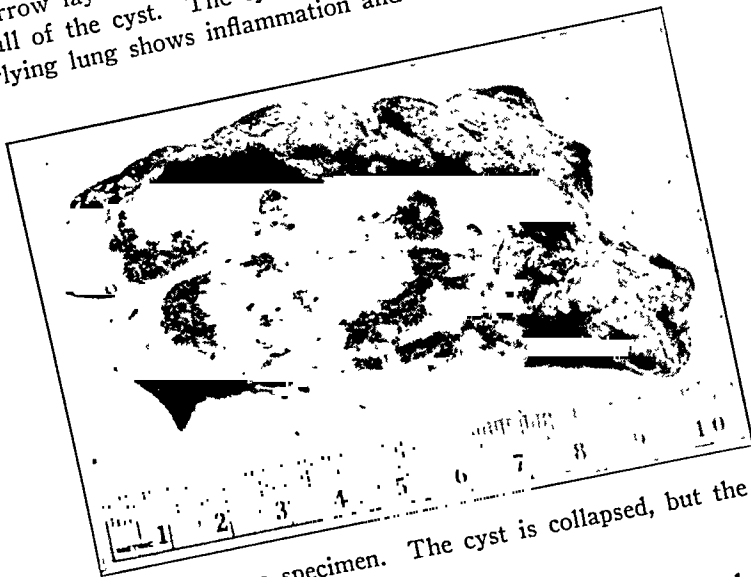


Fig. 3 (case 1).—Gross specimen. The cyst is collapsed, but the communicating cavities are seen.

alveoli and relative isolation of bronchi. Eosinophils are profusely distributed in the inflamed lining. The inflammation seems of greater duration than the clinical history would indicate.

The child has been asymptomatic since. On March 1, 1947, when last seen, he was well and his lungs were clear on physical and roentgenographic examination.

*Summary*.—A 13 week old child underwent excision of the upper and middle lobes of the right lung for multilocular cysts of the upper lobe. Despite absence of fever or signs of respiratory infection and despite the brief history, the cyst was infected and there were extensive inflammatory changes. The child has been well ever since.

*CASE 2*.—V. W., a white male infant, was 12 months of age at the time of operation. He had always eaten poorly and had gained little weight. From the time he was 5 months old he suffered one mild respiratory attack after another. He was hospitalized for two and a half months, being discharged when he was 10 months old. Shortly thereafter he had a severe respiratory infection called bronchitis. Since then he had gone progressively downhill.

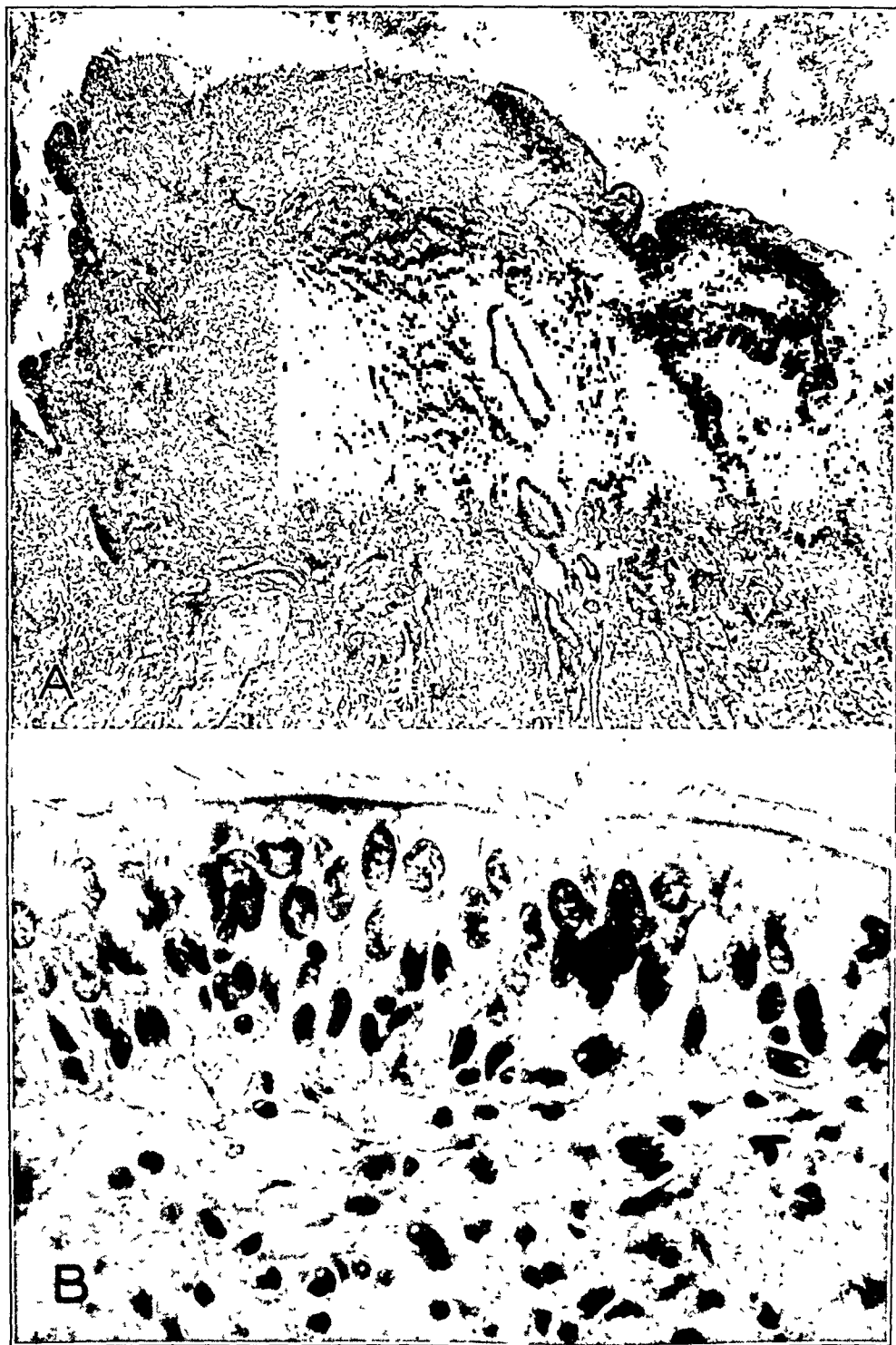


Fig. 4 (case 1).—*A*, photomicrograph of cyst wall;  $\times 30$ . Most of the cyst wall is well preserved, and the basement membrane and lamellated fibrous tissue walls are plain. The smooth muscle is not visible with this power. Although the child was only 13 weeks old and had no clinical signs of infection, one area of the cyst wall is extensively ulcerated. The subjacent lung is greatly scarred. *B*, photomicrograph of cyst lining;  $\times 600$ . The cilia of the pseudostratified columnar epithelium show plainly.

He was a thin, underdeveloped infant with pale skin and mucous membranes. There was no clubbing of the fingers. Over the left side of the chest was a wide area of increased percussion resonance and decreased breath sounds.

A roentgenogram (fig. 5) showed marked displacement of the heart and mediastinum to the right, with air in a large cyst occupying almost the entire left side of the chest. The left region of the diaphragm was displaced downward. In the bronchogram the left main bronchus was seen to end abruptly. There appeared to be no fluid in the cyst.

The preoperative impression was of a cyst in the upper lobe of the left lung.

*Operation* (July 16, 1946; excision of the lower lobe of the left lung, Dr. Ravitch).—The left hemithorax was found to be entirely filled by a large, round, smooth, bluish, thick-walled cyst containing air. The cyst was aspirated of 230 cc. of air. Even immediately after this aspiration it was not empty but was small enough to be delivered into the wound. It refilled rapidly with air, and it finally proved necessary to leave a large needle in situ. The cyst proved to involve the entire lower lobe of the left lung, while the upper lobe was completely atelectatic and displaced into the mediastinum. After removal of the lower lobe, the upper lobe expanded readily and filled the hemithorax.

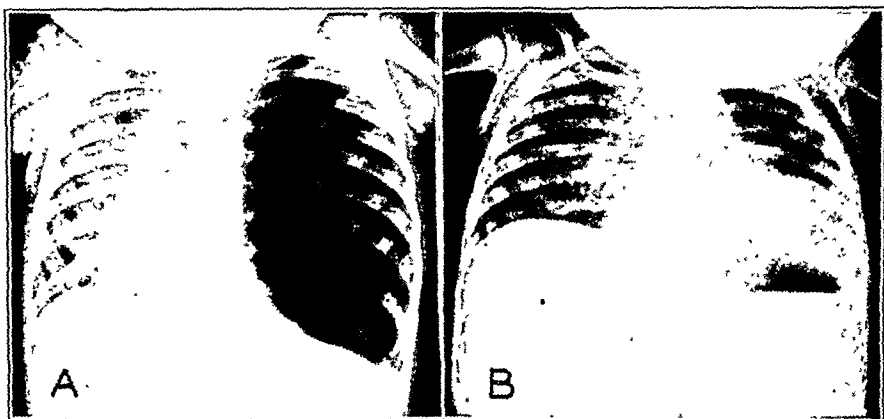


Fig. 5 (case 2).—The preoperative roentgenogram (A) shows the left hemithorax filled by an air-containing cyst which crosses the mediastinum and displaces the heart. B, three weeks after lobectomy. There is a little residual pleural thickening at the base of the left lung, the heart is back in position and the upper lobe of the left lung has expanded.

For several days after operation air accumulated in the left side of the chest. Otherwise the convalescence was smooth, and the lobe expanded well.

*Pathologic Report.*—The removed lobe is almost entirely occupied by a large, thin-walled, delicate cyst (fig. 6). Such epithelial lining as is left is low cuboidal. There is a thin smooth muscle layer and no visible mucous glands. The surrounding lung is scarred and compressed, forming a thin layer around the cyst. Here and there are fibrous septums projecting into the lumen like polypi (fig. 7). In a few places the cyst wall shows acute inflammation.

*Course.*—When last heard from, in November 1946, the patient was well.

*Summary.*—A year old infant had a huge air cyst of the lower lobe of the left lung filling the left side of the chest and displacing the mediastinum. Lobectomy was performed. A one-way valve action was demonstrated at operation. Complete recovery resulted.

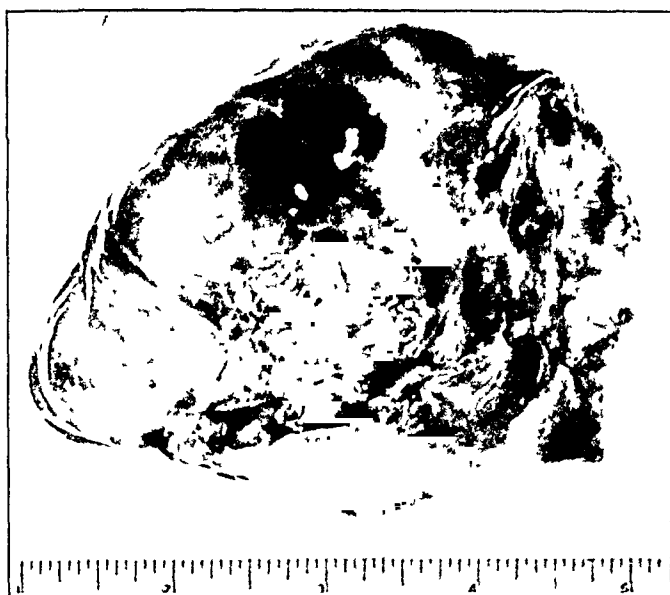


Fig. 6 (case 2).—Gross specimen. The cyst occupies all but a small segment of the basal portion of the lower lobe of the left lung.

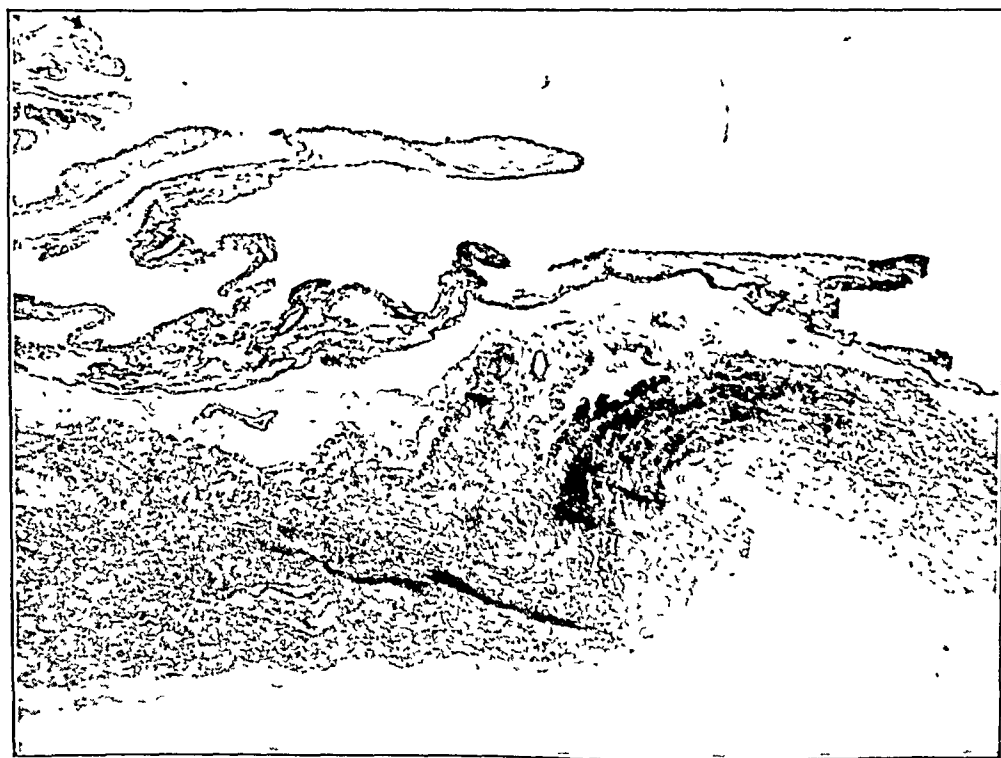


Fig. 7. (case 2).—Photomicrograph of cyst wall and lung;  $\times 30$ . Full thickness of lung and cyst wall. The pleura is thickened and the lung collapsed and scarred. The cyst wall is thin. The epithelium lining the cyst is rather flat and covers the numerous septums which appear in the section almost like polypoid projections.

CASE 3.—D. C., a white female infant, was 8 months old on admission to the hospital. The baby weighed 6 pounds (2.7 Kg.) at birth but for the first week was too feeble to suck and had to be spoon fed. At 4 months she weighed 11 pounds (5 Kg.). There had been occasional attacks of spontaneous cyanosis, a few minutes at a time, up to the age of 4 months, when she had cough, fever and dyspnea, diagnosed as pneumonia. The roentgenogram showed multiple air cysts in the right upper area of the chest. Her temperature rose irregularly after subsidence of the first episode. Two months before admission to the hospital her temperature rose to 102 F. and remained there. A roentgenogram showed fluid-containing cavities in the lung, and multiple aspirations yielded foul pus, from which *Staphylococcus aureus* and nonhemolytic streptococci were cultured. The fluid levels finally disappeared.

On admission she was found to be a thin, weak, severely malnourished infant in no acute distress. The percussion note was dull, and breath sounds were diminished over the upper lobe of the right lung. There was no clubbing of the

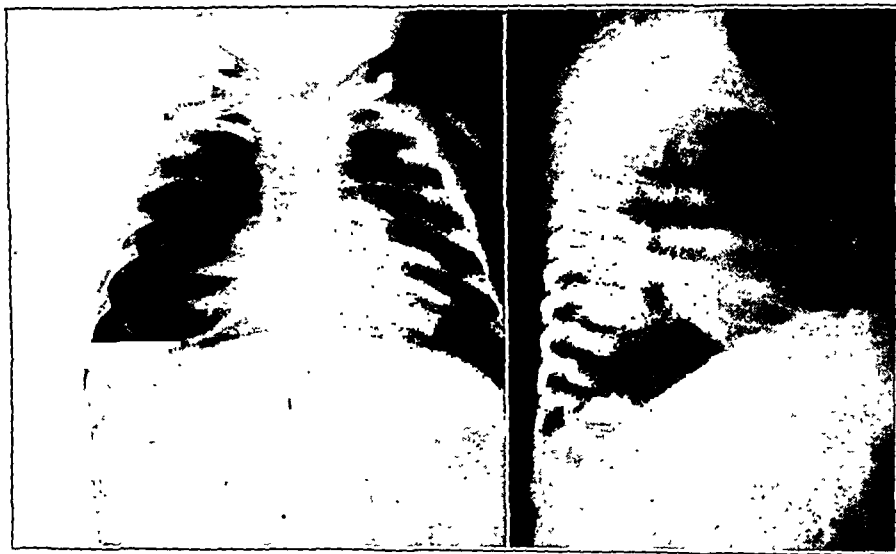


Fig. 8 (case 3).—Roentgenograms, anteroposterior and lateral views. At least two large cysts are seen filling the right hemithorax.

fingers. A roentgenogram (fig. 8) showed the entire right side of the chest filled by large air-containing cysts, with no fluid levels. The heart was displaced to the left.

The child was sent home (September 1939) to be "built up" and to return for operation in two years. However, in one month she died of lobular pneumonia.

*Pathologic Report.*—(The organs were forwarded for study.) The heart and left lung are normal. The lobes of the right lung are fused. At the apex is a large cystic cavity lined by delicate shining membrane. The largest cyst is 5.5 cm. The other cyst, a little smaller, does not communicate with it. The cyst wall is lined by granulation tissue, showing acute and chronic inflammation with occasional epithelial remnants. These are probably remnants of alveoli from the subjacent lung. These epithelial cells are low cuboidal. The substrate is dense scar tissue overlying the lung, which shows chronic inflammation.

*Summary.*—This was an 8 month old infant with severe constitutional symptoms from infected cysts, correctly diagnosed. Operation was deferred, and the patient died of a recrudescence of the pulmonary infection.

CASE 4.—D. N. was a white boy aged 2 years, 11 months. The child was apparently well until 14 months of age, when he had a respiratory infection for two weeks, diagnosed as bronchopneumonia. Two months later he had another bout of fever, dyspnea and malaise, lasting three weeks. For the subsequent six months he had repeated similar attacks, each lasting one or two weeks. He was thought to have unresolved pneumonia or possibly empyema or a pulmonary abscess. The condition was always localized in the right lung. When he was 2 years old a thoracentesis yielded 12 cc. of thick pus, and rib resection and drainage were performed. The cavity healed after a month, but the child soon after abruptly became febrile and the wound broke open and drained pus. There was no sputum.



Fig. 9 (case 4).—Most of the right hemithorax is occupied by the large cyst, which is seen here partially filled with sodium iodide. The intercostal catheter had been inserted elsewhere to drain the "empyema."

Physical examination showed an undernourished child. There was a scar medial to the right scapula and a draining sinus at the level of the scapular spine. Iodized poppyseed oil 40 per cent instilled in the sinus outlined a large cavity occupying the position of the upper lobe (fig. 9). No bronchial communication could be demonstrated. Another rib resection was performed and another catheter inserted. The child coughed up methylene blue which was injected into the cavity.

He returned on October 1933, nineteen months after the onset, with the cavity unchanged and still draining.

*Operation* (Dec. 6, 1933, Dr. Rienhoff).—The smooth-walled cyst in the right lung was excised from the upper lobe by sharp dissection. Convalescence was fairly smooth, although the cavity was still draining at the time of the patient's discharge on Jan. 8, 1934. At present he is reported alive and well.

*Pathologic Report.*—The cyst is a saclike structure, 7 by 5 cm., with a smooth, glistening lining.

Microscopic examination (fig. 10) shows a well preserved epithelial lining varying from tall, ciliated, evenly columnar cells to pseudostratified columnar cells. A well defined basement membrane overlies the dense, scarred, fibrous wall in which are many lymphoid follicles and one lymph node. The adjacent

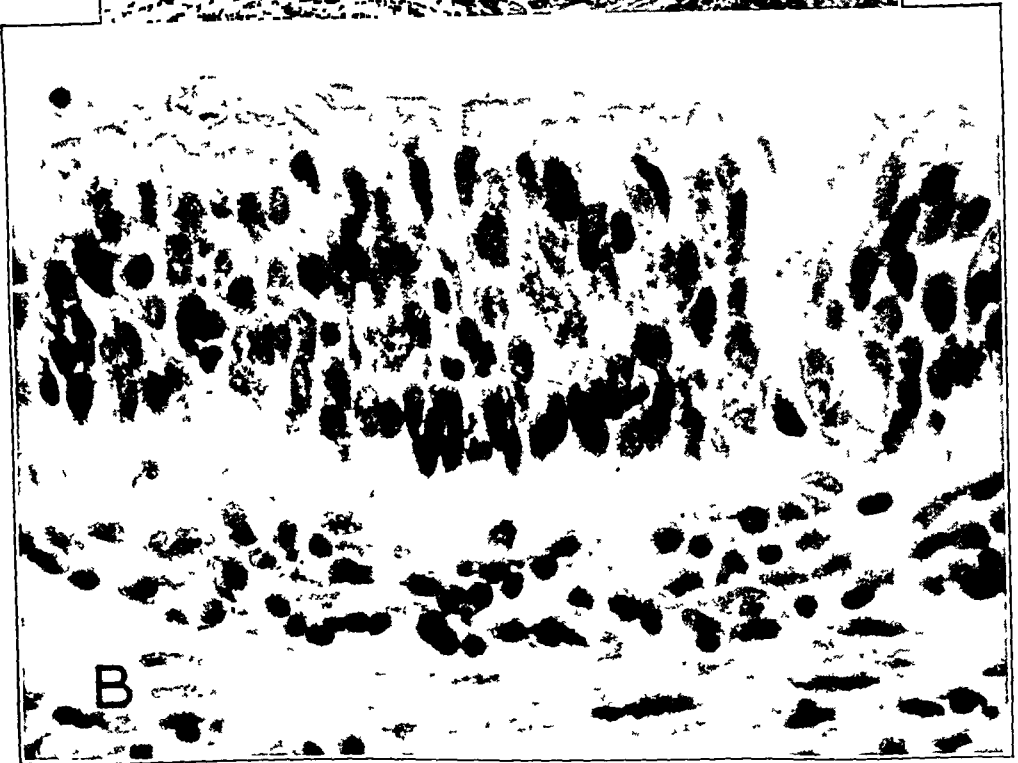
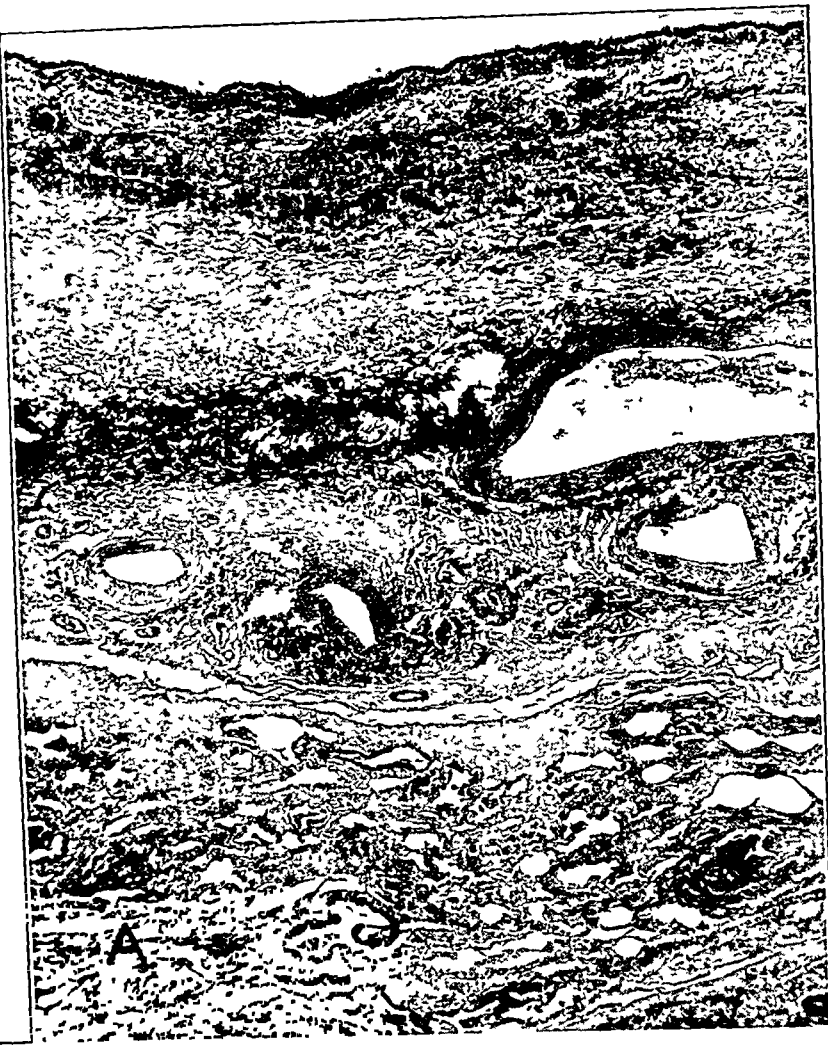


Fig 10 (case 4) —*A*, photomicrograph of cyst wall,  $\times 30$ . The epithelium is well preserved, and beneath it is a thick fibrous wall. It is difficult to tell whether the epithelium-lined spaces in the scarred subjacent lung are small cysts or merely isolated bronchi. *B*, photomicrograph of the cyst lining;  $\times 600$ . The tall pseudostratified columnar epithelium is intact despite two years of catheter drainage



lung is scarred and collapsed, and the numerous bronchi stand out in relief, as well as many irregular spaces, which might be construed as anomalous structures lined by bronchial epithelium.

*Summary.*—The child had been treated for almost two years for supposed chronic empyema, with repeated drainage. Excision of a unilocular cyst and partial resection of the upper lobe of the right lung were performed when the child was 3 years old. Despite the drainage and infection, the lining of the cyst is well preserved

CASE 5.—F. O. was a white boy aged 12 years. Five years before his admission he had a severe respiratory infection, diagnosed as pneumonia and followed by what was thought to be empyema. Six months later a rib resection and open drainage of the putative empyema were performed. A year and a half after

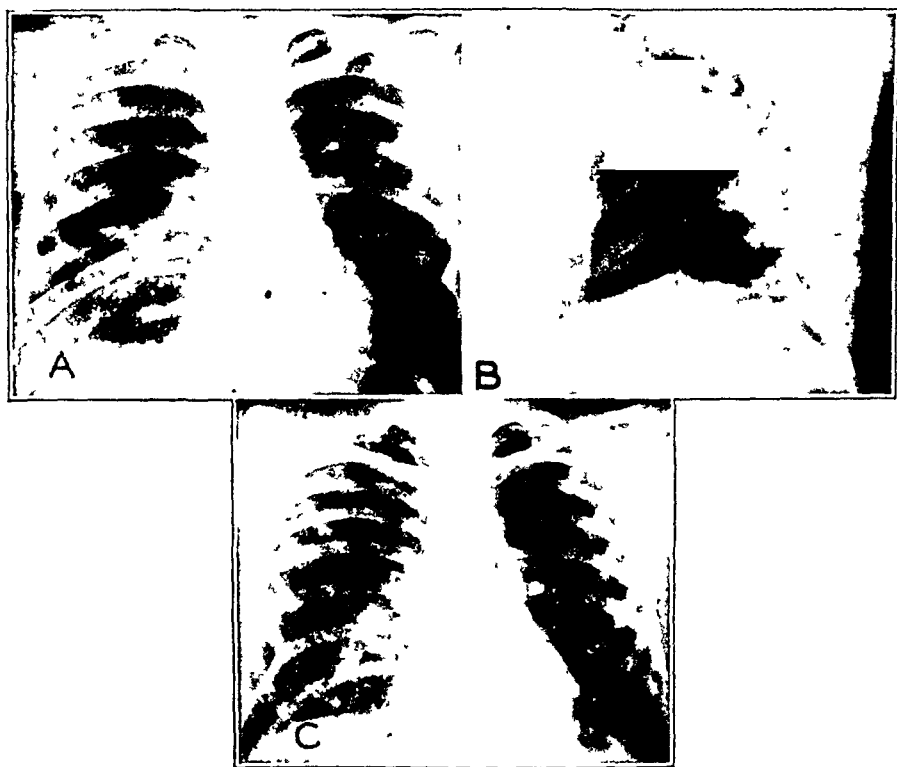


Fig. 11 (case 5).—*A* and *B*, preoperative roentgenograms show the catheter draining multiple radiolucent cystic areas in the lower lobe of the right lung. *C*, postoperative roentgenogram shows only residual pleural thickening.

this the chest was still draining, and a secondary closure of the cavity was attempted. The closure held for two months, when he became febrile, the cavity had to be reopened and for the first time a bronchopleural fistula was recognized. It was closed by cauterization, but the cavity persisted. The roentgenograms (fig. 11) were finally diagnosed as showing congenital cysts of the lung, and the child was sent to the hospital for operation. Iodized poppyseed oil 40 per cent injected into the trachea ran into numerous cysts.

Physical examination showed a vigorous boy of 12 years. There was no clubbing of the fingers. A depressed scar in the right posterior axillary line

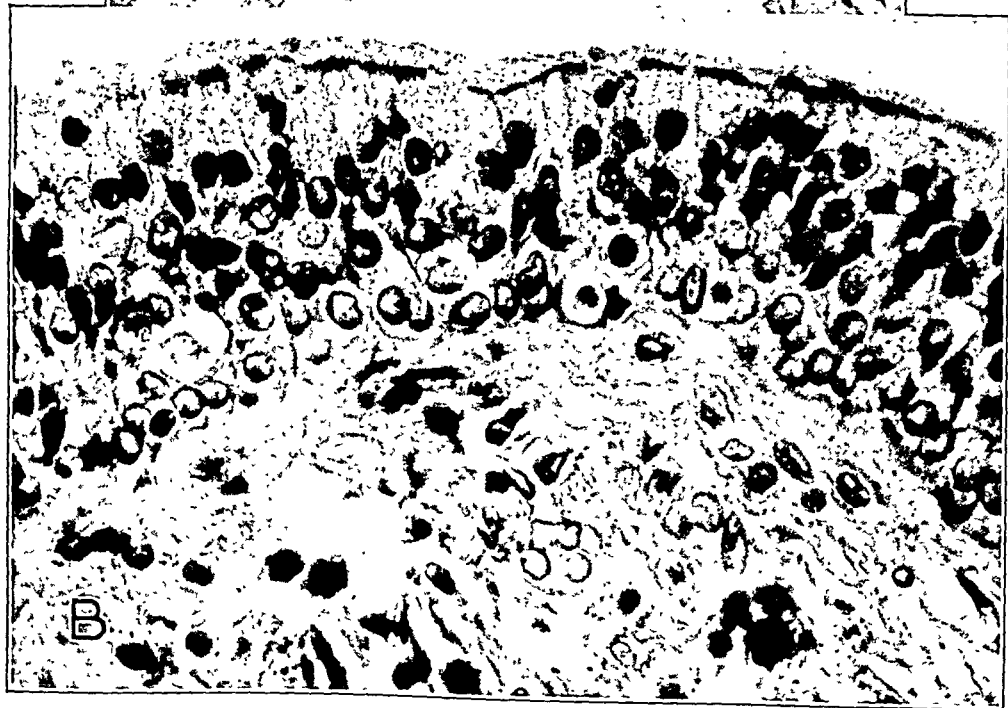


Fig. 12 (case 5).—*A*, photomicrograph of cyst wall and lung;  $\times 30$ . Well preserved epithelium lines a relatively thin-walled cyst. The pleura is greatly scarred and thickened. *B*, photomicrograph of cyst lining;  $\times 30$ . Pseudostratified columnar ciliated epithelium persists despite four and a half years of open drainage.

along the eighth rib surrounded an almost dry sinus 2 cm. in diameter leading into the chest. Slight dullness and suppression in the region of the scar and poor descent of the right side of the diaphragm were the only physical signs of thoracic disease.

*Operation* (May 13, 1944, Dr. Blalock; removal of the right lower and middle lobes).—The lower lobe alone appeared to be involved, but the middle lobe was removed because it was collapsed and atelectatic. Convalescence was smooth but for delayed expansion of the upper lobe.

*Pathologic Report*.—Just beneath the pleura on the anterolateral and posterolateral surfaces of the lung is a large cavity. When opened, it measures 12 by 15 cm. It is really multilocular, although the secondary cavities are small and mostly shallow and have large openings from the main chamber. The lining is thin, smooth, white and soft. Running along the surface in varying directions and curving and anastomosing in irregular fashion are numerous elevated, thin, cordlike thickenings of the lining. Some of these cords extend across the whole cyst from anterior to posterior and from lateral to posterior surfaces. The general consistency and appearance of these cords and cordlike elevations on the surface of the lining are much like those of the chordae tendineae of the heart valves. In the lumen there is a small amount of slightly opaque, pinkish fluid.

The cyst is lined by pseudostratified ciliated columnar epithelium, beautifully preserved in spite of the years of infection (fig. 12). Under the basement membrane is a layer of fibrous tissue beneath which the lung is only slightly scarred. There is no cartilage in the wall of the cyst, but there are remnants of smooth muscle. In a good many places there are small branches that grow off the main lumen of the cyst like little bronchioles, and these are clearly related to the underlying pulmonary structure.

*Summary*.—A 12 year old boy had a four and a half year history of repeated operations for drainage of an empyema and attempted closure of the cavity. In the lower lobe of the right lung he had a multilocular cyst which was lined by ciliated epithelium. He is well after resection of the lower and middle lobes on the right.

CASE 6.—J. F. was a white boy aged 11 years, 3 months. A cyst of the lung was seen in a roentgenogram taken routinely when the child was in the hospital at 1 year of age for diarrhea. At 5 years of age, during an attack of pneumonia when he was extremely ill with high fever, a tube was inserted in the left side of the chest to drain the cyst. For the succeeding six years the tube was worn continuously. There was a constant slight discharge of glairy fluid, and there were the usual phenomena attendant on a bronchial fistula. He had no other pulmonary symptoms after insertion of the tube.

Physical examination on the patient's admission to the hospital showed a vigorous, well developed and well nourished boy of 11 years. There was a small rubber tube in a sinus in the left fifth interspace in the posterior axillary line. Through this tube a little glairy mucus was discharged, and on forced expiration air could be heard whistling through the tube. Respiratory excursions were diminished on the left, and there was dullness at this base.

Roentgenograms showed (fig. 13) a large, apparently unilocular, air-containing cyst occupying most of the lower lobe of the left lung and drained by a tube. Injection of iodized poppyseed oil 40 per cent into the cyst through the tube demonstrated connection with the bronchi, and a bronchogram demonstrated the cyst.

*Operation* (Oct. 17, 1946, Dr. H. W. Scott).—The cyst was densely adherent to the wall of the chest. When the sinus was clamped off within the

chest, the cyst filled rapidly under tension. Lobectomy was performed. Convalescence was smooth, and the boy was well at the time of discharge.

*Pathologic Report.*—Most of the lower lobe is occupied by a large, unilocular, rather fibrous-walled cyst with a smooth lining. At one point on the anterior surface is a short fistulous tract.

The cyst is lined by bronchial epithelium, tall, ciliated, columnar, with mucous glands beneath the lining (fig. 14 *A*). In several areas in the surrounding lung are large groups of bronchial glands proliferating in what appears to be adenomatous fashion (fig. 14 *B*). In one area these proliferating glands are seen to derive from the lining of the cyst (fig. 14 *B*).

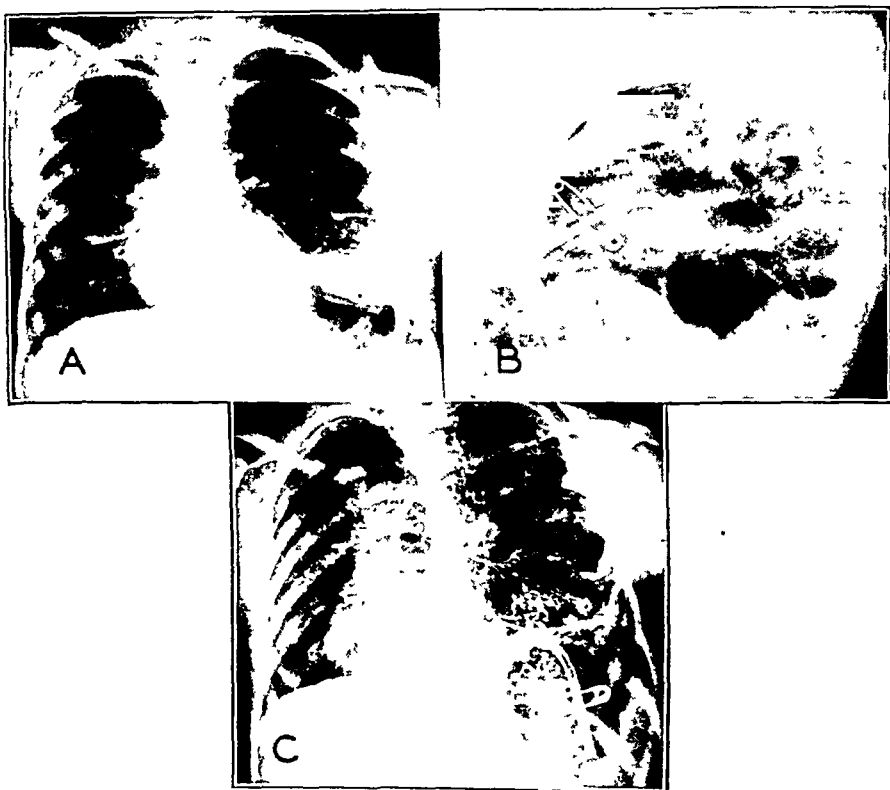


Fig. 13 (case 6).—Iodized poppyseed oil 40 per cent injected through the intercostal tube (*A* and *B*) and injected through the trachea (*C*) showing free communication between cyst and bronchial tree.

*Summary.*—An 11 year old boy was found at the age of 1 year to have a cyst of the lower lobe of the left lung. Frequent attacks of pulmonary infection culminated at the age of 5 in a severe episode, during which the cyst was drained. The drainage tube was maintained for the succeeding six years, with no symptoms but drainage and escape of air. At operation a valvular mechanism was proved. Resection of the lower lobe of the left lung effected a cure. The epithelial lining of the cyst was well preserved despite six years of drainage. Adenomas of mucous glands were found.

CASE 7.—S. W. was a Negro girl aged 9 years. The child's birth and development were normal, and she was thought to be well until two months before her admission to the hospital, when she had what was apparently pneumonia, with a



Fig. 14 (case 6).—*A*, photomicrograph of cyst lining;  $\times 30$ . An adenomatous proliferation of bronchial glands can be seen deriving directly from the lining epithelium. *B*, photomicrograph of lung;  $\times 30$ . Section taken at a distance from the cyst wall shows an area of adenomatous proliferation of mucous glands in the parenchyma of the lung.

temperature of 106 F., pleuritic pains and other symptoms. She recovered on sulfonamide therapy. Five days before admission she again had fever, cough and pain. Physical examination on admission showed a moderately sick girl with a temperature of 100 F. There were dullness and suppression over the lower lobe on the left and under the fluoroscope what was interpreted as dense opacity. Roentgenograms showed multiple radiolucent areas in the region of the lower lobe of the left lung (fig. 15). Her reaction to a tuberculin test was negative, and on penicillin therapy the fever and cough receded. Bronchograms (figs. 15 *B* and *C*)

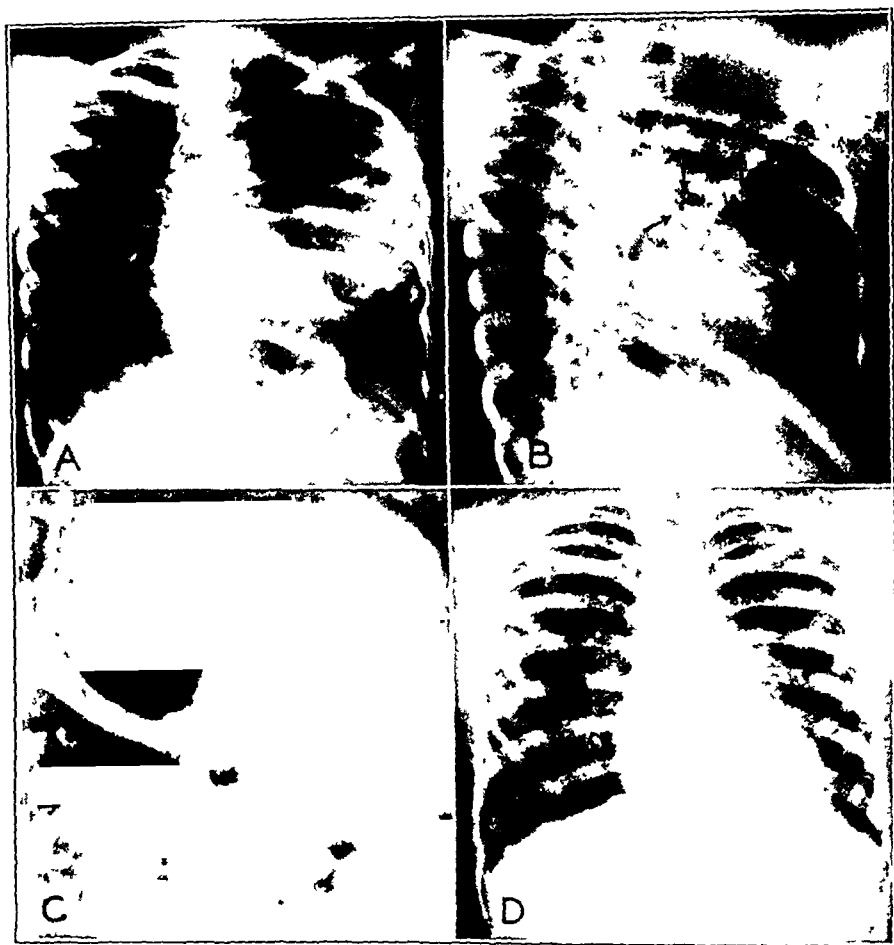


Fig. 15 (case 7)—Preoperative film (*A*) shows multiple cystic areas in the left mid-lung field. Bronchograms (*B* and *C*) show an anomalous bronchus arising from the left main bronchus and coursing upward before the division into upper and lower lobes. In (*B*) some lipiodol® has entered the cysts. The postoperative film (*D*) shows the normal appearance produced by expansion of the small anomalous segment of the upper lobe of the left lung.

showed the cystic areas in what was thought to be the lower lobe and the lingula of the upper lobe filled with iodized poppyseed oil 40 per cent.

*Operation* (Jan. 10, 1946, Dr. Ravitch).—There was found a trilobed left lung with a small upper lobe and two large remaining lobes, both involved in the cystic process. The rudimentary upper lobe was a slender pink structure about 50 by 20 cm. lying along the mediastinum and coming off the main bronchus

independently, its bronchus ascending sharply. This lobe was spared, the two lower lobes which were "about equal in size being removed. The child convalesced satisfactorily, and almost at once the small lobe left behind filled the hemithorax. Fifteen months later the only evidence of her previous difficulty was the intercostal scar. Her chest was clear on physical and roentgenographic examination (fig. 15 D).

*Pathologic Report.*—All the upper lobe is occupied by a large multilocular cyst containing gray mucoid material. There are numerous small cystic areas in the remainder of the lung. Purulent material is present in the bronchi of the lower lobe, much of which has relatively normal parenchyma.

The cyst is lined by bronchial epithelium, some almost squamous and some ciliated. The walls were scarred with multiple septums which look, in section,



Fig 16 (case 7).—Photomicrograph of the cyst wall;  $\times 30$ . The lining epithelium is intact, and one sees several cysts with connecting trabeculations. The underlying lung is scarred. Where the cyst wall is seen at a distance from a septum or trabeculation it is delicate.

like polypoid projections (fig. 16). Some of the scarring and organization in the lung is within the lumen of the bronchioles. Eosinophils are fairly numerous. Here and there a few smooth muscle fibers remain in the scarred cyst wall.

*Summary.*—A 9 year old girl suffered repeated attacks of pulmonary infection for two months. A bronchogram showed, in the lower lobe of the left lung, air-containing cysts which were injected with iodized poppyseed oil 40 per cent. At operation a trilobed left lung was found, with a small, uninvolved "upper lobe" coming independently off the main bronchus and corresponding to Brock's apical

and subapical segments. The two lower lobes were removed. Review of the bronchograms (fig. 15 C) shows distinctly an independent upper lobe bronchus coming off the main bronchus before its bifurcation. The pectoral and lingular segments formed the larger part of the remainder of the upper lobe and were the segments chiefly involved in the formation of the large cysts. The small apical segment filled the left side of the chest.

CASE 8—W. B., a Negro boy aged 12½ years, was first seen on July 10, 1946. He had a twenty-four hour history of anorexia and a twelve hour history of pain in the epigastrium and the lower part of the chest. Fever was noticed just before he was brought to the hospital. He had a slight cough for twelve hours. His past history was entirely normal

*Physical Examination.*—The temperature was 103 F. and the white blood cell count 10,000. The patient was a moderately ill Negro boy with signs of infection of the lower lobe on the left, diminished breath sounds, fine rales and diminished resonance.

Fluoroscopy showed an opaque area in the lower lobe of the left lung, with a fluid level. A roentgenogram (fig. 17 A) showed a dense infiltration extend-

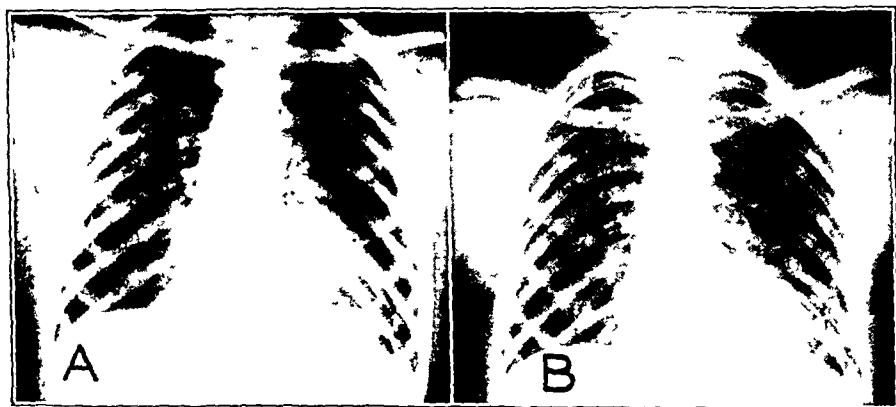


Fig. 17 (case 8).—A, roentgenogram showing fluid level in a radiolucent area in the lower lobe of the left lung. B, bronchogram; the lower lobe bronchi curve around the lesion. In a pulmonary abscess bronchi would tend to end abruptly at the lesion.

ing from the left hilus into the lower pulmonary fields. There was a radiolucent area within the area of consolidation representing a cavity with a fluid level. Bronchograms (fig. 17 B) showed the mass in the lower lobe displacing the bronchi. No iodized oil entered the cavity.

He was treated with postural drainage, penicillin aerosol and bronchoscopic aspiration on the supposition that he had an abscess of the lung. He was afebrile and asymptomatic by the sixth day, but treatment was continued for three more weeks, and on his discharge from the hospital he was asymptomatic although the roentgenograms were unchanged. He returned to school but was readmitted a month later with a slight nonproductive cough. Bronchoscopic findings and bronchograms were unchanged. It was thought that he might have an infected cyst of the lower lobe of the left lung

*Operation* (Sept. 27, 1946, Dr. Scott and Dr. Ravitch).—The lower lobe of the left lung was found densely bound down to the diaphragm and the wall of the chest, from which it was cleared by sharp dissection. Three large separate arteries, varying in diameter from 4 to 6 mm, were found to enter the convexity



of the lower lobe posteriorly and were readily traced to their emergence from the aorta. These anomalous systemic vessels arising in a row from the aorta at intervals of a centimeter were each larger than the usual pulmonary artery to the lower lobe. The vessels were ligated and divided. There was no fissure between what were thought to be the lower and upper lobes, and after the bronchus and the vein had been secured (no ordinary pulmonary artery was seen with any certainty) the lobe was resected on clamps. It was now disclosed that although this left a portion of lung about as large as the usual upper lobe, there was an additional and separate lobe, completely distinct and not at all adherent. It was clear that we were dealing with a trilobed left lung. Reexamination of the preoperative bronchograms showed that there was an anomalous upper lobe bronchus coming off the left main bronchus before the dichotomous division into lower and upper. The anomalous lobe appeared to consist of Brock's apical and subapical divisions. The larger lobe adherent to the lower lobe was apparently composed of the pectoral and lingular divisions. The lower lobe was removed. Injection of the anomalous arteries produced a relatively normal pulmonary arteriogram, reversed in direction, all the fluid running readily out of the pulmonary vein at the hilus (fig. 18A).

The absence of any fissure between the lower lobe and the upper lobe produced a large raw surface. This was covered with interrupted sutures. It was then found that this so distorted the lobe that about a third of it could not be inflated. Therefore, the sutures were cut one by one until the lobe had expanded completely. This was a striking example of the occasional disadvantage derived from suture of the cut surface of the lung, a point emphasized by Churchill.

After operation the patient was initially febrile; thereafter, convalescence was uneventful.

*Pathologic Report.*—The specimen is a lower lobe of the left lung. The surface is rough and ragged, and on one side is a broad area of cut lung. On the convexity are three substantial arteries about 4 to 5 mm. in diameter, said to have arisen from the aorta. Within the lobe is a cavity filled with thick pus, the surrounding lung extensively indurated. The lining of this cavity proves to be ciliated epithelium, with many mucous glands in and under it in the surrounding layer of smooth muscle (fig. 18B). Although in some areas the lining is ulcerated and in one area there is a lining of granulation tissue, elsewhere the epithelium is perfectly preserved. Within the cyst and on its wall are seen particles of coal pigment. The subjacent lung is scarred and shows little but bronchial elements which frequently appear cystic and seem to be proliferating.

*Summary.*—A 12 year old boy with a brief history of pulmonary suppurative disease was found to have a cavity in the lower lobe of the left lung. At operation for cyst of the lung, suspected because of the persistence of the cavity after the infection had entirely subsided, he was found to have a trilobed left lung, the cavity being in the lowermost lobe and this lobe obtaining most or all of its arterial supply from three large anomalous vessels arising from the descending aorta and entering the convexity of the lower lobe. He has been asymptomatic since removal of the lobe.

CASE 9.—P. L. was a white boy aged 6 years, 5 months. At the age of 9 months he was seen at another hospital for pneumonia, which lasted three weeks. At 3 years he had fever and "bronchitis," and ever since he had cough at night and morning sputum, which he would swallow. Three months before his admission to the hospital he had two episodes of vomiting at night. "Often

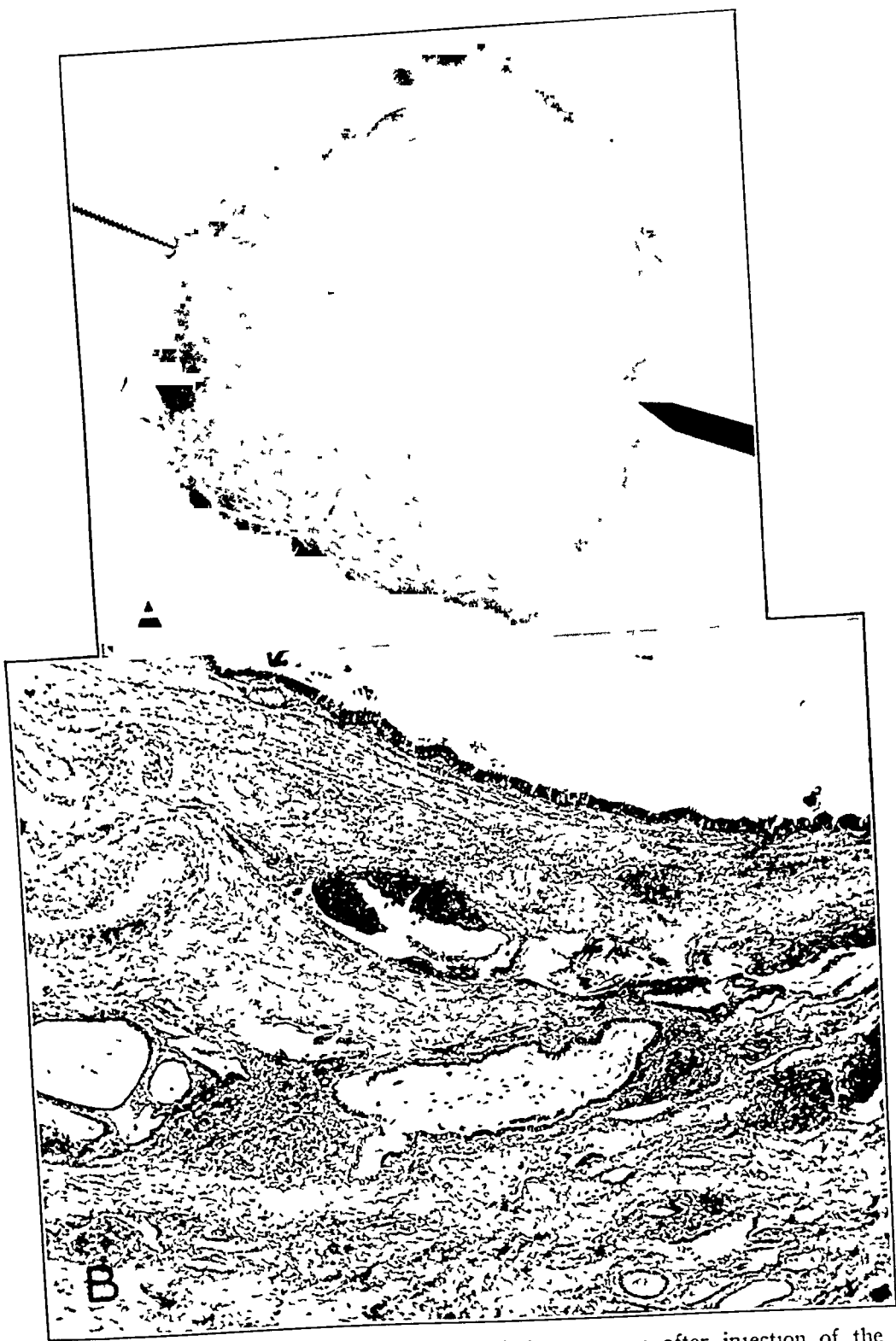


Fig 18 (case 8) —*A*, roentgenogram of the specimen after injection of the largest anomalous artery with Hill's mass (by Dr. George Duncan). The hemostat is on the pulmonary vein at the hilus of the lobe. The orientation of the arteries is seen to be the reverse of the ordinary pattern. *B*, photomicrograph of cyst wall and subjacent lung;  $\times 30$ . The characteristic epithelial lining is seen. Beneath the fibrous wall and apparently between it and the lung parenchyma are several cystic spaces lined with bronchial epithelium. The arrow points to a mucous gland beneath the cyst epithelium.

after doing somersaults he would cough up a greenish-whitish shimmering lump of material." The cough was worse at night, and often he had had bouts of dyspnea and noisy respirations.

Physical examination showed a fairly well nourished boy with a constant moist cough. There were diminished resonance and impaired breath sounds over the lower lobe on the right. A few fine post-tussic rales were audible. On fluoroscopy there was increased density at the right base, with two large round areas of radiolucency. The sputum contained type 14 pneumococcus.

Roentgenograms (fig. 19) showed at least three large cavities with fluid levels in the right lower lobe of the right lung. On bronchoscopy, greenish pus was seen to emerge from the bronchus of the lower lobe on the right. Alpha strep-

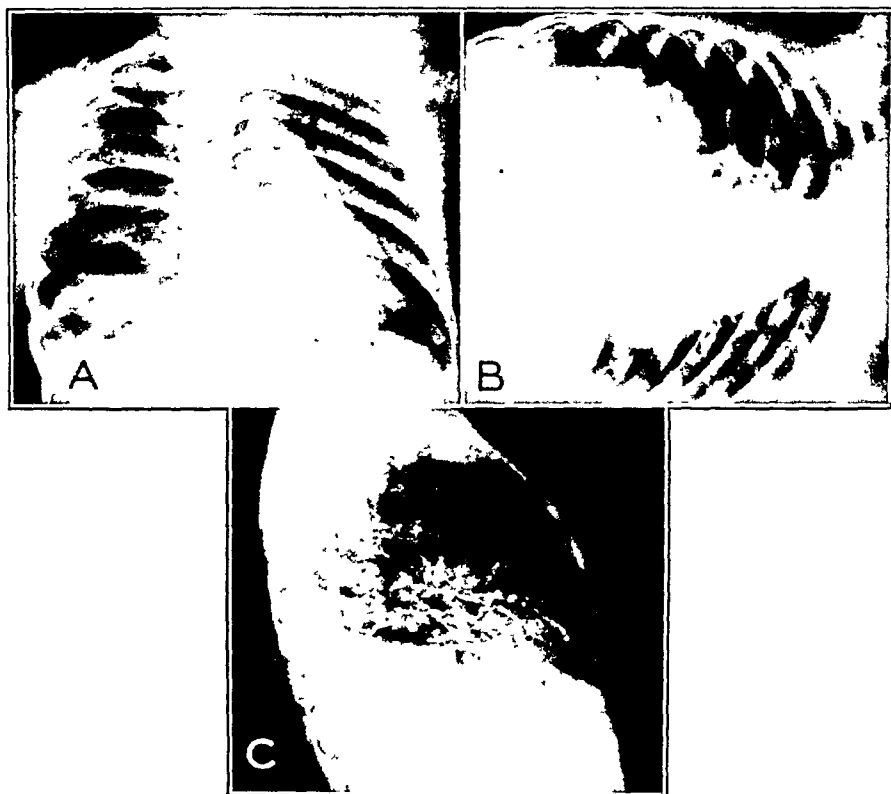


Fig. 19 (case 9).—Roentgenograms (*A* and *B*) of patient in upright and left lateral decubitus positions show fluid levels in cysts in the lower lobe of the right lung. Bronchogram (*C*) shows that lipiodol® does not enter the cysts.

tococci were cultered from the pus. Bronchograms (fig. 19 *C*) showed lateral displacement of the bronchi, with abrupt termination of the smaller bronchi. Iodized oil did not enter the cavities.

*Operation* (Sept. 27, 1946, Dr. Ravitch).—The lower lobe of the right lung was excised. A large systemic vessel, apparently arising from an intercostal artery, entered the convexity of the posterolateral surface of the lower lobe. However, there was found the usual pulmonary arterial branch to the lower lobe in its normal position. Recovery was uncomplicated.

*Pathologic Report*.—The specimen is a lower lobe of the right lung, firm and almost solid in many areas, with others rounded, cystic and bulging. A 5 mm.

artery enters the convexity of the posterolateral surface. On section the lobe is found to be almost entirely replaced by numerous large cysts, many of them intercommunicating (fig. 20) and all of them filled with thick glairy pus. In addition to the large cysts, 4 to 5 cm. in diameter, which were those seen in the roentgenograms, there are numerous smaller ones. The specimen was lost, and no microscopic sections were made.

*Summary.*—A 6 year old boy had a history of pulmonary infection from the age of 9 months. In the roentgenogram numerous cysts were seen in the lower lobe of the right lung, displacing and obstructing bronchi. At operation the lobe was removed and found to be replaced by cysts. An anomalous systemic vessel



Fig. 20 (case 9).—Gross specimen. The larger cysts intercommunicate, and bronchi can be traced into them. All the cysts contain thick glairy mucus.

arose from an intercostal artery and entered the convexity of the lobe. The boy has been well since operation.

CASE 10.—J. M. was a white girl aged 10 years. At the age of 5 years this child, who had had frequent sore throats and head colds, had a mild nonproductive cough and a low grade fever. In the next six to eight months the cough became productive of thick yellowish sputum. She had been in bed for months at a time ever since. Diagnosis of bronchiectasis of the upper lobe of the right lung was made elsewhere.

Physical examination showed a sallow, chronically ill, unhappy girl of 10 years. She was tachypneic and cyanotic at rest and had decided clubbing of the fingers and toes. Her respirations were labored, accessory muscles being used even at

rest. There were rhonchi in the right upper region of the chest and crepitant rales over both upper lobes, most notable on the right.

Roentgenograms showed clouding of the antrums and the ethmoid bones. Both pulmonary fields showed extensive infiltrative and fibrotic changes (fig. 21 *A*). Bronchograms (fig. 21 *B*) showed extensive saccular formations in the upper lobe of the right lung, with a pronounced tubular bronchiectasis of the lower lobe on the left and similar but less apparent changes in the lower lobe on the right.

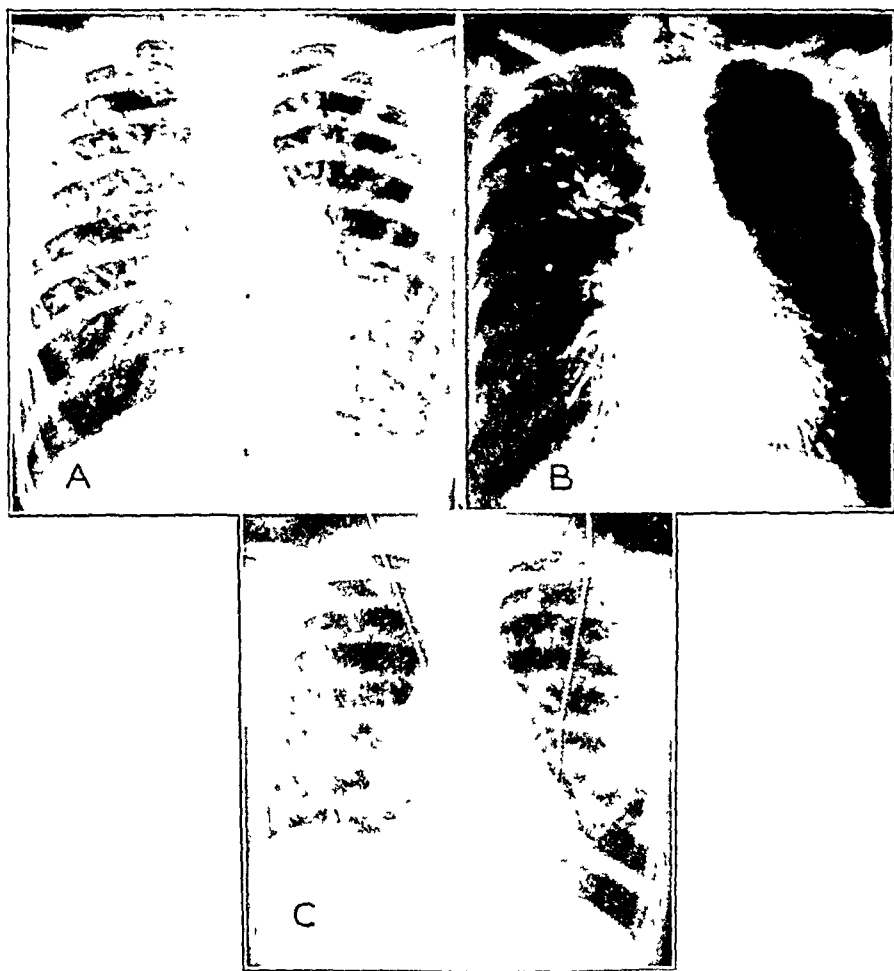


Fig. 21 (case 10).—Roentgenogram on admission (*A*) shows extensive infiltration in both lungs. Bronchogram (*B*) shows cystic bronchiectasis of the right upper lobe and bilateral tubular bronchiectasis of the lower lobes thought to be secondary to the process in the upper lobe. *C*, roentgenogram ten months after removal of the right upper and middle lobes. The chest is essentially clear.

It was impossible to be certain of the middle lobe. The patient was treated for six weeks with postural drainage, expectorants, steam inhalations, penicillin aerosol and penicillin intramuscularly and repeated bronchoscopic aspirations. Her sputum decreased, cyanosis and dyspnea lessened, fever disappeared and roentgenograms of the chest looked less frightening. Her vital capacity rose from 400

to 1,700 cc. It was thought that she had a congenital type of cystic bronchiectasis of the upper lobe of the right lung.

*Operation* (July 15, 1946, Dr. Ravitch).—Excision of the upper and middle lobes of the right lung was performed. The convalescence was smooth and the patient has made excellent recovery since, with practically normal exercise tolerance. She goes to school, rides a bicycle and has unrestricted activity. She has no sputum and almost no cough and shows no cyanosis or dyspnea. The clubbing of the fingers has receded considerably. Roentgenograms taken ten months after operation are essentially clear (fig. 21 C), and it begins to look as if the secondary bronchiectasis might regress without further operation.

*Pathologic Report.*—The lung is largely atelectatic, and numerous large bronchial spaces are seen. There are no features of the microscopic appearance affording certain differentiation from bronchiectasis. However, there are numerous large

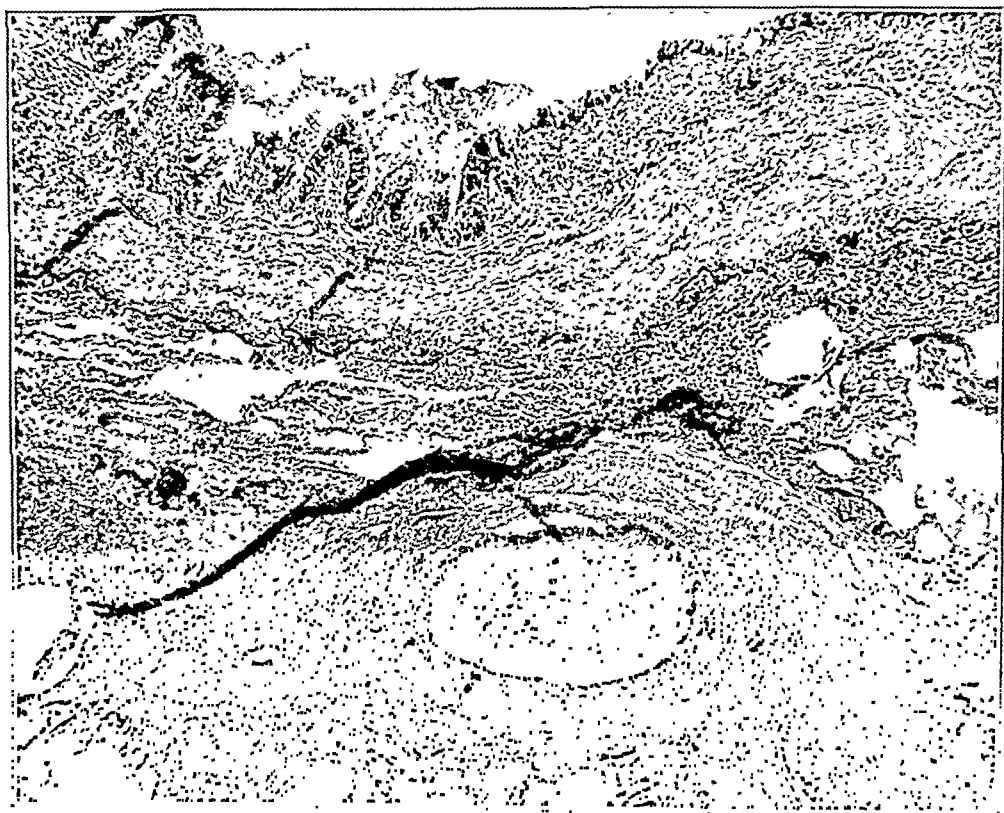


Fig. 22 (case 10).—Photomicrograph of a cyst wall;  $\times 10$ . Typical bronchial mucosa. This is a large cavity, but no cartilage was seen in its wall. The occurrence of such smaller cystic spaces as seen in the photograph is at least suggestive.

bronchial spaces lined by infolded bronchial epithelium with remarkably little evidence of infection. Several large bronchus-like structures show no cartilage (fig. 22).

*Summary.*—A 10 year old girl had a five year history of cough and pulmonary disease. Roentgenograms showed a cystic type of bronchiectasis in an unusual location, the upper lobe of the right lung. Because of the location and the character of the cystic areas we thought we must be dealing with true congenital bronchiectasis or a type of cystic disease and not any ordinary secondary bronchi-

ectasis. The lower lobes on both sides showed a good deal of tubular bronchiectasis, which has subsided, in good part, since the removal of the principal offending lobe.

CASE 11.—H. H. was a white girl aged 6 years. She was first seen at the age of 20 months in September 1942 with a temperature of 103.8 F. and a twelve hour history of grunting respirations. She had had a "cold" for five days. There were physical and roentgenographic signs of pneumonia of the right lung, and she was admitted to another hospital. There a positive reaction to a tuberculin test was reported, and she was sent to a tuberculosis sanatorium, where she remained for six months. Her father was tuberculous.

She was seen again in October 1943 for a routine check-up. Physical examination revealed nothing abnormal, but roentgenograms showed fibrosis of the right apex, interpreted as being probably due to tuberculosis. Subsequent roent-



Fig. 23 (case 11).—*A*, roentgenogram; there is dense infiltration in the region of the upper lobe of the right lung. *B*, bronchogram; the cystic bronchiectasis is limited to the upper lobe of the right lung.

genograms showed repeated infiltration of the upper lobe of the right lung, which, it was felt in the tuberculosis clinic, was not due to tuberculosis. The child was puny and poorly developed and had a constant cough. Over a space of three years the lesion persisted, as shown in numerous roentgenograms (fig. 23). The first bronchograms, taken in November 1946, showed extensive cystic or saccular dilations branching out from the main bronchial tree of the upper lobe of the right lung (fig. 23 *B*). There was no demonstrable disease of other segments. Bronchoscopy showed reddening of the mucous membranes on the right.

*Operation* (Jan. 20, 1947, Dr. H. W. Scott).—Resection of the upper lobe of the right lung was performed. Convalescence was uneventful, and the child has remained well since.

*Pathologic Report*.—The specimen is an upper lobe of the right lung which on section shows numerous dilated bronchi containing purulent material. The picture is indistinguishable from bronchiectasis on the basis of the microscopic examination. There are numerous large bronchus-like tubes in scarred lung.

The bronchial lining is well preserved, with little active inflammation and remarkably extensive epithelial infolding. In addition, in some areas there are numerous small round epithelium-lined spaces, probably regenerated alveoli (fig. 24). These are lined with low cuboidal epithelium and again show a surprising lack of inflammation.

*Summary.*—A 6 year old girl had symptoms of suppurative disease of the upper lobe of the right lung for more than four years. Bronchograms showed numerous saccules hanging from the bronchi of the main upper lobe like grapes from a stem. The picture was strikingly similar to that in case 10. We interpret the condition in both cases as congenital cystic bronchiectasis.

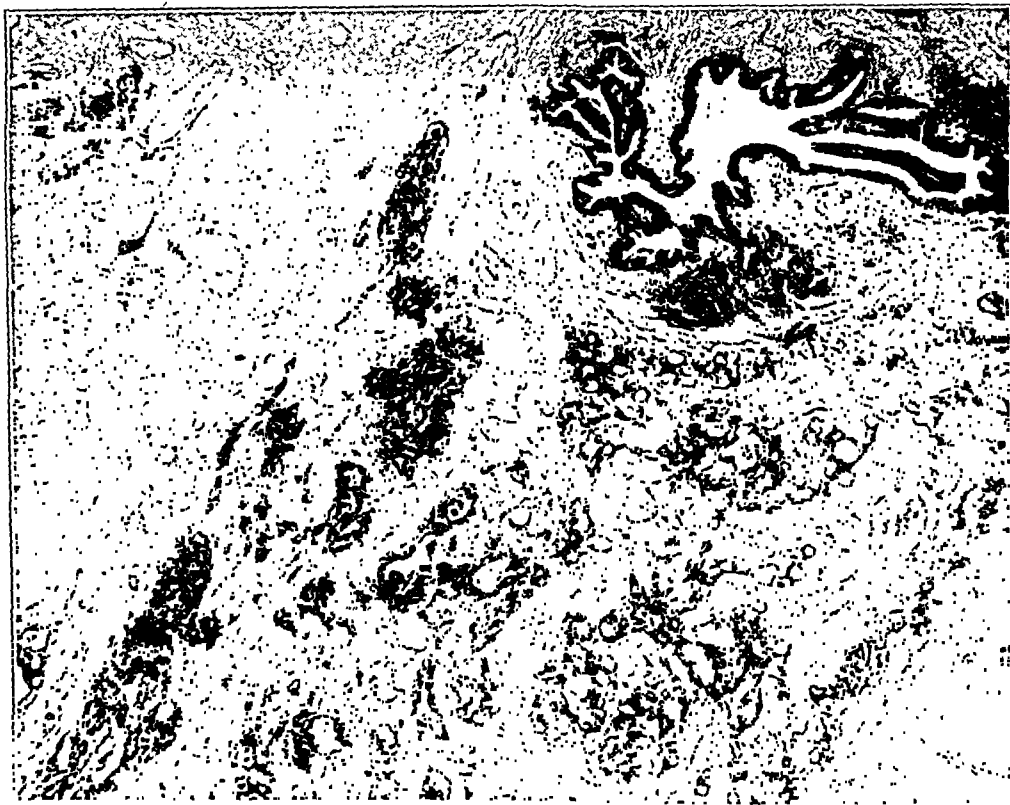


Fig. 24 (case 11).—Photomicrograph;  $\times 30$ . Extensive infolding of the epithelium of the apparent bronchus. In the surrounding scarred lung are numerous cystic spaces which are probably regenerated alveoli. There is little evidence of active inflammation.

CASE 12.—R. H. was a white boy aged 13 years. At the age of 2 years he was alleged to have had pertussis and measles followed by bronchopneumonia. Ever since he had had a severe cough, productive of yellow sputum, particularly in the mornings. He had had a lifelong exertional dyspnea.

Five years before his admission to this hospital roentgenograms were said to show a pathologic process. He was never treated. He had had intermittent respiratory infections confining him to bed. His fingers had been clubbed as long as he could remember.

Physical examination showed a fairly vigorous boy of 13, slightly cyanotic, with rapid respirations (24 per minute) and pronounced clubbing of the fingers.



There was a slight respiratory lag on the left. The percussion note was impaired all over the left side, and the diaphragm in this area was elevated and fixed. Tactile fremitus was increased on the left, and there were whispered pectoriloquy and tubular breath sounds. A clicking noise was heard at the mouth. There were groaning, leathery rales all over the left region of the chest. The patient produced abundant sputum, from which were cultured *Escherichia coli*, *Micrococcus catarrhalis* and streptococci.

Röntgenograms (fig. 25) showed multiple, overlapping, round, radiolucent areas occupying the entire left lung and varying in size from 2 to 4 cm. A bronchogram (fig. 25 *B*) showed many of these cystic cavities filled with iodized oil.

*Operation* (March 30, 1946, Dr. Blalock).—Pneumonectomy was performed on the left side. The pleural cavity was found to be obliterated by dense adhesions. Recovery was rapid and uncomplicated.

The boy was last seen on Nov. 15, 1946. He had no cough, the clubbing had entirely disappeared and he played football with no undue dyspnea.

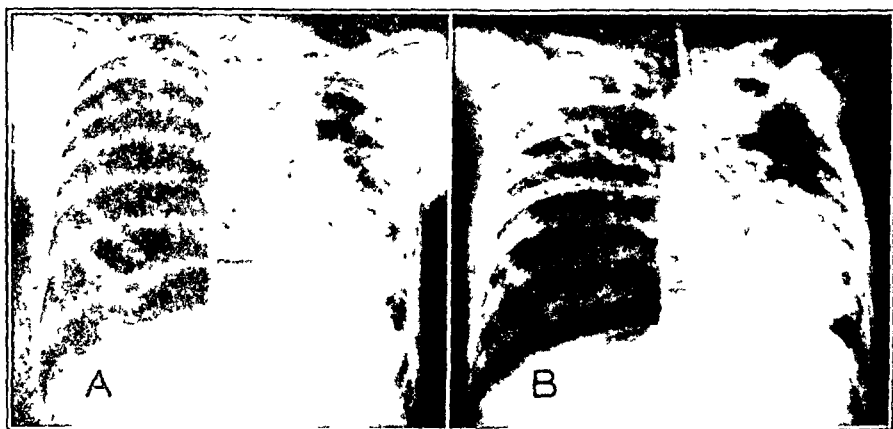


Fig. 25 (case 12).—Roentgenogram (*A*); the left lung is replaced by overlapping cysts. The lung is contracted and the heart drawn to the left. Bronchogram (*B*); several of the cysts closest to the hilus are filled with lipiodol.<sup>6</sup>

*Pathologic Report.*—The specimen is a left lung, the pleural surfaces thickened and shaggy. The lung is firm and yellowish and shows numerous greatly dilated bronchi.

Microscopic examination shows numerous large spaces lined with well preserved bronchial epithelium, remarkably infolded. Definite bronchial glands are seen in some of these spaces. There are tremendous lymphoid infiltration and dense scarring around these structures. Despite the great size of these spaces none of them shows any cartilage in their walls (fig. 26).

*Summary.*—A 13 year old boy had pulmonary symptoms of considerable severity since the age of 2. Growth and development were not interfered with, as one would have expected them to be in bronchiectasis of this degree. The disease was entirely unilateral. The bronchogram of the right side was normal. The left lung was replaced entirely by innumerable cysts. Pneumonectomy was performed on the left side, with alleviation of all symptoms and disappearance of pulmonary osteoarthropathy.

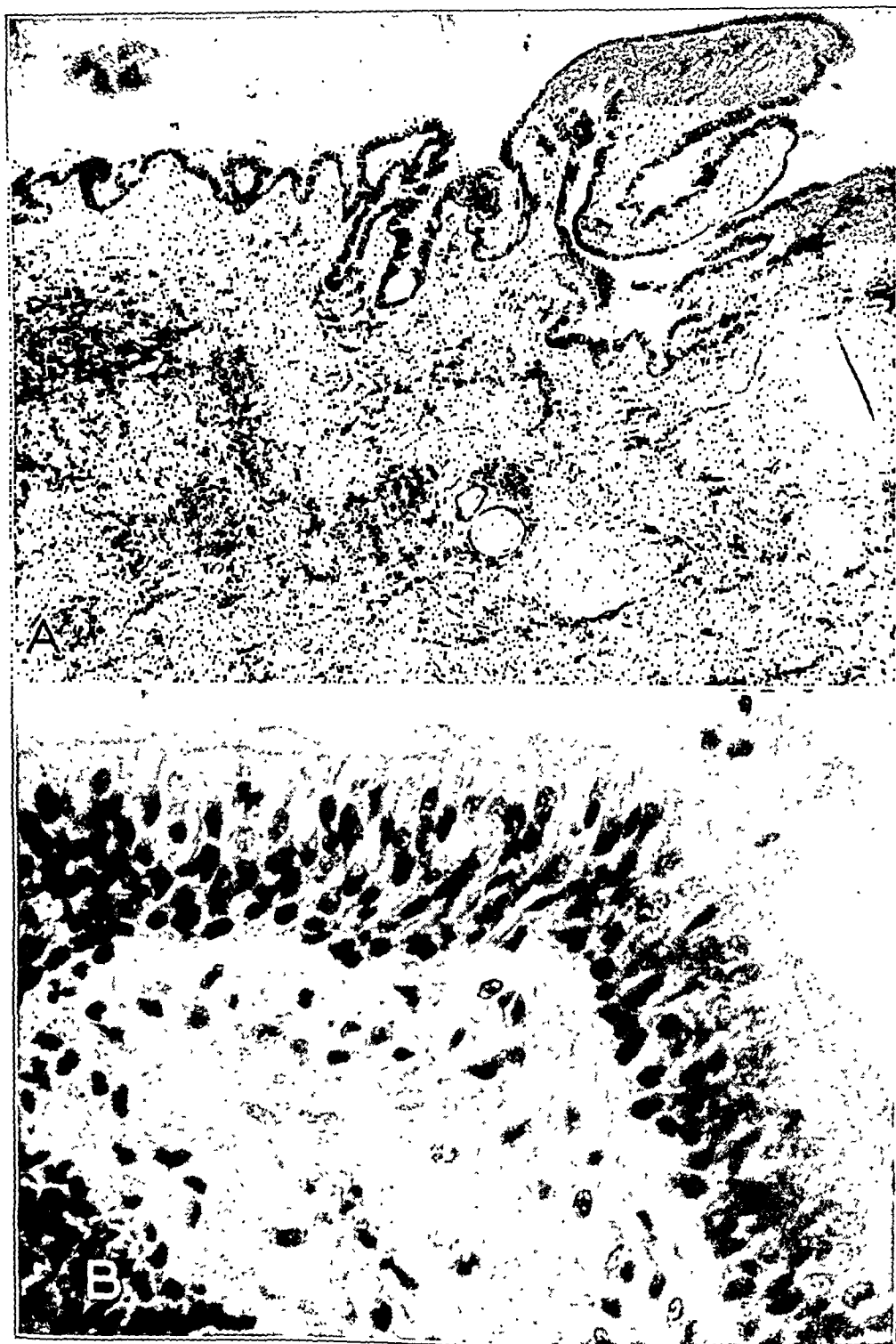


Fig. 26 (case 12).—*A*, photomicrograph of cyst wall;  $\times 30$ . The almost polypoid character of the cyst walls is seen. The epithelium is well preserved and the lung beneath scarred. Although this is a large cyst there is no cartilage in its wall. *B*, photomicrograph of cyst lining;  $\times 600$ . The epithelium is pseudostratified, tall and columnar and in this instance not definitely ciliated.

NOTE.—An additional patient has been operated on since this report was submitted. This was a 3 month old white male infant with cystic disease of the lower lobe of the right lung in whom it was necessary to perform pneumonectomy. The patient has done well since operation.

#### SUMMARY

Twelve patients suffering from cystic disease of the lungs are presented. They varied in age from 13 weeks to 13 years.

Some degree of infection was found in each case.

Eleven of the twelve patients were successfully treated by surgical removal of the involved area of lung (six single lobectomies, four lobectomies of two adjacent lobes and one pneumonectomy).

The single death, from pneumonia, occurred in an infant of 8 months for whom operation had been deferred and was not performed.

Among these 12 patients, 2 were found to have cysts associated with anomalous lobes of the lung, in each instance a trilobed left lung; 1 of these had an anomalous arterial blood supply derived from the aorta. A third patient had an anomalous systemic artery entering a cystic lower lobe of the right lung.

Resection of the cyst or of the cyst-bearing segment of lung is the recommended treatment.

## BLEEDING PEPTIC ULCER

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BALTIMORE

**A**MONG the many wound stripes incident to modern civilization perhaps the one which looms most prominent yet remains most perplexing is the problem of peptic ulcer and its perilous complications. About 8,800 persons die annually in the United States alone from the sequelae of peptic ulcer, and massive hemorrhage due to ulcer is a grim contributor to this excessive toll.

Recent therapeutic procedures in the treatment of peptic ulcer have produced many changes of opinion. However, there still remains much controversy over the treatment of gastroduodenal bleeding. Is surgery indicated and, if so, for which patients? When is the optimal time to operate and what is the operation of choice? What is the present status of transfusions and parenterally administered fluids? Is morphine contraindicated? Is it best to feed patients promptly or to starve them? What is the current trend in antacid therapy? Are amino acids helpful? Is vagotomy the sovereign remedy in bleeding peptic ulcer?

In regard to none of these important issues is there general unanimity of opinion. Dogmas which were formerly held in high esteem have now been discarded, only to be supplanted by doctrines which long ago were regarded with doubt and distrust. Every case of hemorrhage caused by ulcer must be considered on its own merits. There are no hard and fast rules for prudent guidance, as clinical judgment is based on individual experience. However, data collected from mass statistics call attention to the best results of treatment and favor medical progress toward this general attainment.

Thus, the present misgivings concern many phases of the problem of bleeding ulcer—the origin and nature of the lesion itself, the status of medical and surgical treatment, the present prospect for a permanent cure and the successful management of the common complications of peptic ulcer, namely, massive hemorrhage, perforation, obstruction and alkalosis.

The present study of bleeding peptic ulcer is based on a statistical analysis of all patients with gross hemorrhage from an ulcer who have

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From the Department of Surgery, Johns Hopkins Hospital.

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been admitted to the Johns Hopkins Hospital since 1928, that is, all patients with the exception of infants and children who were seen in the pediatric wards with acute gastroduodenal ulcers and massive exsanguinating hemorrhages. These youngsters had acute ulcers of a distinctive type (perhaps analogous to Cushing's or Curling's ulcer in an adult), but the picture presented was otherwise unlike the characteristic clinical picture which we associate with chronic peptic ulcer. Instances of acute erosions of the gastroduodenal mucosa were eliminated from this study whenever this diagnosis was suspected.

From a review of the medical literature it is evident that there is a great divergence of concept regarding treatment and even a greater claim and counterclaim of mortality rates among the champions of a cherished type of therapy for hemorrhage due to ulcer. Certainly much of this difference of opinion must result from the comparison of collected cases which are not at all similar in the severity of the bleeding. In recognition of this fact alone, efforts are constantly being made to discover a more exact method of determining true loss of blood. Only then can a real assessment of the progress of bleeding ulcer be ascertained and reliable evaluation of contrasting measures of treatment be accurately judged. Also, the possible development of newer diagnostic aids which will foretell the location of an ulcer and estimate the caliber of the artery bleeding in its base would be of great value in determining the type of therapy best suited to this imminent source of danger.

#### INCIDENCE

By definition all patients in this series had gross hemorrhage from ulcer in contrast to occult bleeding. Spontaneous vomiting of "coffee ground" material, red blood or the passage of a black, tarry stool depended for quantity on the extent and severity of the hemorrhage. Although it has been shown by several investigators that as little as 60 cc. of ingested blood can be sufficient to cause a tarry stool, yet the average patient hospitalized because of a bleeding peptic ulcer usually showed a much more pronounced degree of loss of blood.

In the period between 1928 and the first part of 1946 (table 1) there were 2,400 patients admitted to the Johns Hopkins Hospital with a diagnosis of duodenal, gastric or marginal ulcer. Many of these patients were admitted to the hospital many times; however, the number of patients, and not the number of admissions, was tabulated. During this same period there were 218 patients with active hemorrhage from ulcer admitted to the hospital. Thus, about 9 per cent of patients with ulcer who required admission to the hospital did so because of gross hemorrhage. This corresponds reasonably well with the reports from other large medical centers. Kirsner and Palmer at the University of Chicago

reported an incidence of massive hemorrhage of 10.6 per cent, Eusterman reported gross hemorrhage in 17 per cent of the operative cases of ulcer at the Mayo Clinic and Heuer noted that 21 per cent of the patients with ulcers admitted to the New York Hospital entered chiefly because of hemorrhage. It is, of course, difficult to estimate the actual incidence of bleeding from ulcer as only about 10 or 20 per cent of all ulcer-bearing patients ever find it necessary to be hospitalized.

*Annual Incidence.*—In figure 1 the annual number of patients with bleeding ulcer are charted according to the yearly rate of admission to the hospital. During the period 1928 to 1935 the catalogue of diagnoses appears to be incomplete and the total number of cases of hemorrhage from ulcer is probably fragmentary. However, from the annual rate of admissions it could not be concluded that the mental and physical strain of World War II predisposed patients with ulcer to increased hemorrhage.

TABLE 1.—*Patients with Ulcer Admitted to the Johns Hopkins Hospital Between 1928 and 1946*

Ulcer		Bleeding Ulcer
1,510	Duodenal.....	156
833	Gastric.....	25
57	Marginal.....	5
.....	Combined.....	8
.....	Unknown.....	24
Total	2,400	218

*Monthly Incidence.*—It is, of course, widely known that the pangs of peptic ulcer are less prevalent during the summer months, and this is also reflected in the lowered incidence of hemorrhage from ulcer (fig. 2). Definite seasonal exacerbations are known to occur in duodenal ulcer during the early spring, late fall and early winter months. The reason for this seasonal periodicity has never been satisfactorily explained, although Crohn and Schwartzman expressed the belief that massive hemorrhage from ulcer may be due to a local Schwartzman phenomenon from infections of the upper respiratory tract, which are most common during the spring and late fall. Lisa and Likely reported 5 cases of chronic peptic ulcer and death from exsanguinating hemorrhage in which bacterial infection of the wall of an artery was demonstrated in each case. Harkins in 1938 studied the problem of acute ulcer of the duodenum as a complication of burns—the eponymic Curling's ulcer—and reported its relation to sepsis.

## RACE AND SEX

The sex incidence (fig. 3) among the present series reveals the proportion of males to females in the whole group to be 5.2 to 1. However, it is of interest to note that of the 16 patients who died 15 were males and only 1 was a female.

The ratio of white to Negroes was 2.3 to 1, which may be explained by an equivalent difference in the bed capacity at the Johns Hopkins

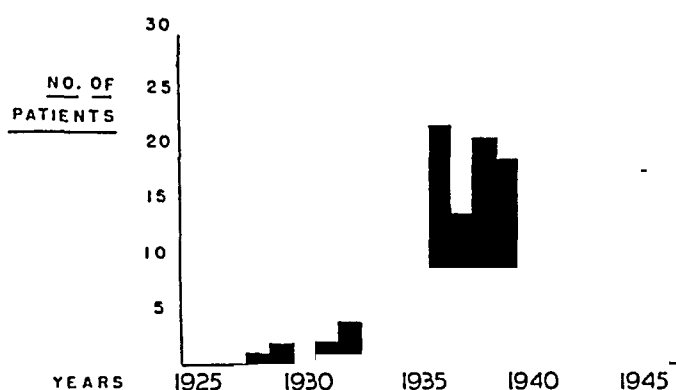


Fig. 1.—The period from 1935 to 1946 probably represents a more accurate record of the annual number of patients with bleeding peptic ulcer admitted to the hospital.

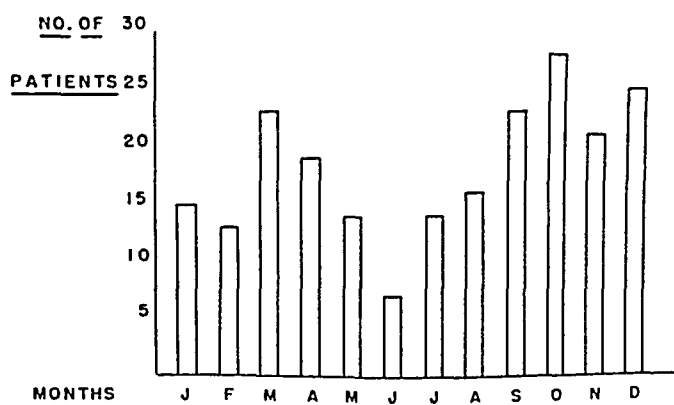


Fig. 2.—Seasonal exacerbations are known to occur in peptic ulcer, and this fluctuation is also reflected in the monthly admissions of patients with hemorrhage from ulcer.

Hospital for the respective races or perhaps accounted for by the racial distribution of Baltimore, which is approximately in the proportion of 4 whites to 1 Negro.

## AGE

Among the varied factors which affect the seriousness of hemorrhage from ulcer age has been shown by many investigators to be highly impor-

tant. Experience at the Johns Hopkins Hospital (fig. 4) corroborates the fact that hemorrhage from ulcer is more likely to be serious or fatal among patients past 50; in 150 patients under the age of 50 the mortality rate was only 5.3 per cent, whereas in 68 patients above the age of 50 the mortality rate was more than doubled—11.8 per cent. However, it is important to note that there were 8 fatalities among patients under the age

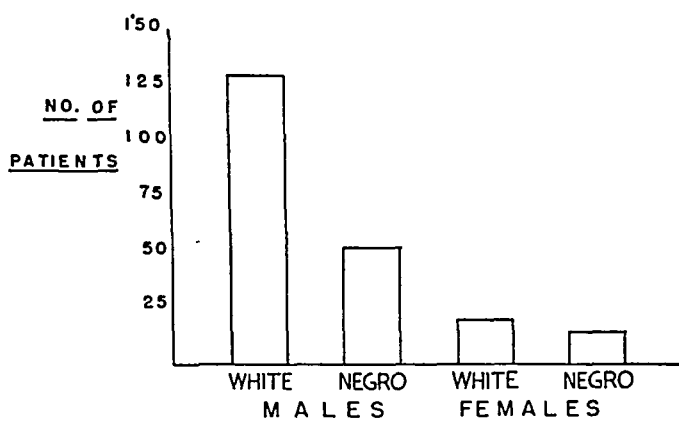


Fig. 3.—The proportion of males to females in the entire group is 5.2 to 1. However, it is of interest to note that of the 16 patients who died, 15 were males and only 1 was a female.

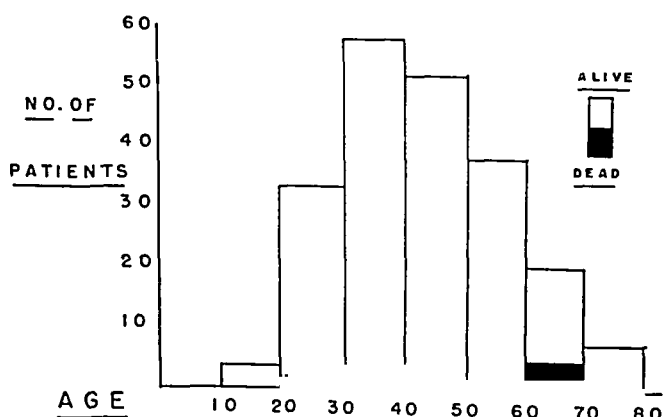


Fig. 4.—In 150 patients with bleeding peptic ulcer who were under the age of 50 the mortality rate was only 5.3 per cent, whereas in 68 patients above the age of 50 the mortality rate was 11.8 per cent. The highest mortality rate occurred in the sixth decade.

age of 50, and that 4 of these died while comparatively young, i. e., while in their thirties. Thus, even young patients with elastic arteries may die of hemorrhage from ulcer, for youth alone is no guarantee of hemostasis.

Most cases of hemorrhage from ulcer occurred in the third decade of life. However, more than half of the entire series (112 patients) ranged in age between 30 and 50 years.



## BLEEDING

The exact assessment of the severity of hemorrhage from ulcer is by no means easy. The amount of blood vomited or passed through the bowel can rarely be accurately measured. Thus, since there are no precise criteria for the classification of early hemorrhage the present group of cases was divided grossly according to (1) available laboratory tests, (2) the clinical picture and (3) the house staff's recorded impression of the amount of blood lost.

It has been shown by Blalock and others working in the field of shock that loss of blood or plasma is a most significant initiating factor in the production of shock. A decreased blood volume and reduced circulation caused by massive or prolonged hemorrhage from ulcer bring about the various physiologic and clinical changes which are the sustaining factors in shock. Copious bleeding leads to tissue anoxia, increased capillary permeability and irreversible peripheral circulatory collapse. Fatal shock, with characteristic hemoconcentration and pathologic changes in the tissues, can be produced even by slow persistent bleeding.

TABLE 2.—*Extent of Bleeding Among Patients with Ulcer*

	Number	Deaths	Per Cent
Moderate.....	83	2	2.4
Massive.....	102	12	11.7
Minimal.....	32	2	6.2
Unknown.....	1	0	...

It does not seem to matter whether the hemorrhage is outside the body or into the gastrointestinal tract, as in cases of bleeding ulcer, as far as the production of shock is concerned.

In the absence of simple and reliable methods of determining the effective circulating blood volume, clinical judgment alone is difficult and estimation of true loss of blood (when determined early) may even be misleading. The initial blood counts and hemoglobin determinations are not accurate indexes of the severity of bleeding because it may be several days before blood volume can be again restored to normal and only then can the magnitude of actual loss of blood be measured. Clinical signs of reduced blood volume are mainly to be found in alterations of blood pressure and impaired physiologic functions incident to a decreased blood flow.

In the present series (table 2) gross hemorrhage from ulcer was divided into three groups: moderate, massive and minimal, depending primarily on the stated impression of the severity of the loss of blood as recorded in the history. This means of classification was further verified by the clinical condition of the patient and the routine laboratory studies

of the blood. In accordance with every reasonable expectation, the highest mortality rate occurred in the group of cases in which the hemorrhage was classified qualitatively as massive.

#### AZOTEMIA

Greater vigilance and clinical alertness in the medical observation of cases of bleeding ulcer may be augmented by estimation of the increase in blood urea. Often the simple cases of hemorrhage from ulcer may be sifted from the severe cases by means of this helpful expedient. Massive hemorrhage into the gastrointestinal tract causes an increase of blood urea occasionally to uremic levels. There is usually oliguria and sometimes anuria. The urine may show a good concentration of urea, but the specific gravity is not as high as might be expected.

Although the actual mechanism of this alteration of blood chemistry is obscure, it has been reported by some observers that the rise in blood urea closely parallels the degree of hemorrhage into the intestinal tract. Borst attributed the azotemia to the rapid absorption of urea formed from the blood in the intestinal tract. However, Johnson administered whole blood by stomach tube in amounts up to 1,500 cc. and noted a marked increase of blood urea in only 1 patient, who had impaired renal function.

Witts expressed the belief that the increase is due to the fall in blood volume which reduces the blood flow through the kidneys. This occurs at a time when the kidneys have the extra work of excreting a large amount of nitrogenous products derived from blood which is in the intestine. Yet, other investigators found the rise of blood urea nitrogen less closely related to the severity of the hematemesis, melena or anemia. Regardless of the uncertainty of its origin, the azotemia usually occurs promptly within the first day or two of hemorrhage from ulcer and may be used, within limits, as a guide in charting the course and management of a bleeding peptic ulcer. It appears probable that the azotemia is due to the combined effects of reduced blood volume, lowered blood pressure, the dehydration associated with hemorrhage from ulcer and the added waste products from the breakdown of blood.

#### PAIN

Several of the British surgeons, among them notably Gordon-Taylor, have stressed the importance of severe or intractable pain as a precursor of ill-boding in cases of hemorrhage from ulcer. The presence of excruciating pain preceding active bleeding and persisting afterward is considered a bad omen, and its prognostic significance favors urgent and early surgical intervention during the period of active hemorrhage. From the experience in this hospital (table 3) one cannot confirm this

belief or even conclude that severe pain is a Cassandra in cases of hemorrhage. Little significant difference in mortality statistics was noted regardless of whether severe pain was present or not.

### HISTORY OF ULCER

In the present series of 218 patients with hemorrhage from peptic ulcer (table 4) more than 75 per cent gave a characteristic clinical syndrome of typical chronic ulcer. Less than 25 per cent failed to give an orthodox history of ulcer prior to the onset of bleeding but were found to have an ulcer on further careful study or at operation.

Although it is more or less commonly believed that the mortality rate increases with each recurring hemorrhage from ulcer, the present series

TABLE 3.—*Relation of Pain to Mortality*

	Number	Deaths	Per Cent Mortality
Severe pain with bleeding.....	66	6	9.0
Severe pain before or after bleeding....	4	0	0.0
No severe pain.....	147	10	6.8
Unknown.....	1	0	0.0

TABLE 4.—*History of Ulcer* \*

Previous ulcer history.....	165
No previous ulcer history.....	53
Previous history of bleeding ulcer.....	108
No previous history of bleeding ulcer.....	108
Unknown.....	2

\* Patients whose history indicated recurrent hemorrhage had about the same fatality rate as those admitted during their first attack of bleeding.

fails to verify this belief. Patients whose history indicated recurrent hemorrhages had about the same fatality rate as those admitted during their first attack of bleeding. Kirsner and Palmer found that "the mortality rate was approximately as high in the first hemorrhage as in subsequent hemorrhages." Allen and Benedict reported that "60 per cent of our fatal cases died during their first episode of bleeding." Thus, although it has been rather a hackneyed dogma to say that no patient ever dies from his first hemorrhage from ulcer, the facts belie the truth of this specious reasoning.

### DIAGNOSIS

The difficulties encountered in the differential diagnosis of gastroduodenal bleeding are apparently more perplexing to the medical writers of other countries than they are to American physicians. Holman, from a study of cases of bleeding ulcer at the New York Hospital,

stated that "the commonest cause of bleeding from the stomach or duodenum is peptic ulcer, and this diagnosis can usually be made after such other possible causes as esophageal varices, cancer and the hemorrhagic diatheses have been excluded." On the other hand, Witts, Physician in Charge of Medicine at St. Bartholomew's Hospital in London, found that gastroduodenal bleeding was due to peptic ulcer in only 37 per cent of the cases and in the remainder of the group it was due to acute erosion, gastritis and cirrhosis.

Perhaps the fact that it is difficult to distinguish accurately between gastritis, acute erosions and chronic ulcers has been responsible for certain discrepancies noted in the reports of so-called comparable series of cases of bleeding ulcer. There can be no doubt that in cases of hemorrhage resulting from acute erosion or gastritis the mortality is negligible, whereas in cases of hemorrhage from chronic ulcer the mor-

TABLE 5.—*Complications Among Patients with Bleeding Ulcer*

	Number	Deaths	Per Cent Mortality
Obstruction.....	22	2	9.0
Severe anemia.....	108	13	12.0
Slight anemia.....	110	3	2.7
Arteriosclerosis.....	53	9	16.9
No arteriosclerosis.....	165	7	4.2

tality is high. Gastritis appears to be far more common in England and the continental countries than in this country, and by its very nature and its great similarity to the clinical picture of chronic ulcer it may often be mistaken for it. Gastroscopy alone settles the diagnosis, but in the presence of gastroduodenal bleeding such a procedure is not without hazard.

#### COMPLICATIONS

It is needless to say that in dealing with bleeding peptic ulcer it is of the utmost importance to determine, if possible, in which case hemorrhage from ulcer is likely to cause death if unchecked by surgical intervention and, conversely, which ulcer will cease to produce hemorrhage under proper conservative therapy. In pursuit of an answer to this problem, several common complications of bleeding ulcer were studied and their respective mortality rates determined (table 5).

Pyloric obstruction causing considerable retention of gastric contents and evidenced clinically by vomiting or by visible gastric peristalsis or objectively demonstrated by roentgen examination caused no significant increase in the death rate.

Serious hemorrhage causing severe anemia as contrasted with slight anemia (3,000,000 red blood cells, with hemoglobin 50 per cent, or 7.5 Gm. per hundred cubic centimeters, and the clinical evidences of

prostration and shock being the arbitrary dividing line between severe and slight anemia) caused rather a sharp difference in the mortality rates. Exsanguination causing severe anemia resulted in 13 fatalities in 108 patients, whereas passive bleeding or slight anemia resulted in only 3 deaths in almost the same number of patients, a rather striking difference. Cullinan and Price have suggested that the gradient of the drop in hemoglobin and red blood cell values, rather than the actual values, may indicate more clearly the severity of bleeding. This gradient was not studied in the present series.

Arteriosclerosis, noted in the record of 53 patients, appeared to have rather a profound effect on the mortality rate. However, the fact that brisk hemorrhage may be occurring through an eroded arteriosclerotic artery can be only part of a springtide story. The vicious cycle of impaired renal blood flow, cardiorenal complications and the azotemia of gastrointestinal hemorrhage acts to aggravate further a high mortality rate.

Thus, it seems that the common complications of hemorrhage from ulcer are merely straws in a shifting wind and can be only in a limited sense used as a trustworthy guide in determining the most desirable therapy for the patient with bleeding from a peptic ulcer. Indications for treatment depend on a clearcut classification of the type of bleeding which is encountered. It is unfortunate, however, that such a clearcut clinical criterion designating the specific patient with uncontrollable hemorrhage from ulcer remains yet to be found. Patients enter the hospital in every stage of physical reaction and debility due to hemorrhage. Their physiologic response to loss of blood is notoriously different, and the selection of patients whose hemorrhage is likely to prove fatal if not surgically checked as contrasted with those whose hemorrhage is likely to cease spontaneously is still a problem.

#### TREATMENT

Until recently the treatment of peptic ulcer and its complications was generally conceded to be medical. Differing opinions concerning the etiology and pathogenesis of peptic ulcer naturally resulted in a procession of differing therapeutic panaceas. Many of these enjoyed momentous popularity until a recurrent hemorrhage or ulcer niche was found at the end of the rainbow. The evaluation of any ulcer regimen is difficult because many ulcers heal with little or no treatment. Moreover the clinical course of the disease is characterized by variable periods of remission and exacerbation.

Also, the psychosomatic effect of any new drug may lead to a temporary relief of symptoms and an ensuing period of good health. As pointed out by both Eusterman and Heuer, the general principles of treatment of hemorrhage from ulcer are based on the physiologic treat-

ment of hemorrhage anywhere. Medical management consists of complete physical and mental rest, the frequent feeding of a soft, nutritious diet, administration of antacids, the intravenous use of dextrose, isotonic sodium chloride solution and amino acids, plasma and blood transfusions, sedatives, antispasmodics and narcotics and all other ancillary measures indicated. Whether the current trend toward section of the vagus nerve will alter these basic principles of treatment remains to be seen, for at the moment we are in that interminable "interval between the seed and the timber."

*Medical Treatment.*—Narcotics: Among the more common derivatives of opium, morphine was used most frequently at the Johns Hopkins Hospital to induce quiet and relieve anxiety in patients with hemorrhage from ulcer. Other narcotics administered were codeine, dihydromorphinone hydrochloride, pantopon® (a mixture of the opium alkaloids), meperidine hydrochloride, (demerol hydrochloride®) and Schlesinger's solution (scopolamine hydrobromide, 0.0025; morphine hydrochloride, 0.2; ethylmorphine hydrochloride, 0.4; distilled water, 10). Some caution regarding the use of morphine has been suggested because of its tendency to excite nausea and vomiting and because of its possible harmful effect on an anemic and anoxic respiratory center. However, other investigators have found that it puts the stomach at rest and inhibits gastric secretion. There is ample, experimental evidence to show that atropine sulfate when given generously in conjunction with morphine enhances the inhibition of gastric secretion as well as causes a reduction in the amount of free acid. The liberal use of milder sedatives such as the barbiturates often proves satisfactory in allaying anxiety and restlessness.

*Diet:* Dietary regimens for ulcer and for hemorrhage from ulcer have varied considerably during the course of the past twenty years. Prior to 1934, or shortly thereafter, it was the customary routine at the Johns Hopkins Hospital to place all patients with actively bleeding ulcers on a program of starvation. The experience of Meulengracht and the influence of his results from the prompt feeding regimen have resulted in a decided reversal of medical practice. Although a brief initial period of starvation still remains a common procedure among the members of the more conservative school, the fundamental principle of prompt and frequent feedings now seems to be the rule. It is generally conceded that the orthodox program of prolonged starvation failed to put the stomach at physiologic rest.

The prompt feeding program of Meulengracht offers the patient a diet adequate in calories and vitamins and rich in essential proteins. Frequent feedings administered promptly is the essential element of treatment. As suggested originally by Meulengracht and elaborated on by Raspberry and Miller, the specific type of diet or of antacid medi-

cation is really of secondary importance. Frequent feedings not only aid the patient's nutritional state, reduce free gastric acidity and motility but also bolster his morale and hasten his recovery. The harmful effects of deprivation of food and fluid on a patient bordering on peripheral circulatory failure due to hemorrhage are particularly well shown in table 6. Among 11 patients with hemorrhage from ulcer who were placed on a prolonged and strict program of starvation there were 6 deaths, or a mortality rate of 54 per cent. When contrasted with 76 patients promptly fed a modified Meulengracht diet (six feedings daily of a protein-fortified diet which is low in cellulose), among whom there were no deaths, the results are noteworthy.

TABLE 6.—*Medical Treatment*

	Number	Deaths	Per Cent Mortality
Antacid regimen (Sippy or aluminum hydroxide)...	45	5	11
Starvation .....	11	6	54
Meulengracht diet.....	76	0	0
Andresen diet.....	4	1	25
Total.....	136	12	8.8

TABLE 7.—*Value of Transfusions \**

	Number	Deaths	Per Cent Mortality
Plasma.....	7	1	14.3
Blood (more than 1,000 cc.).....	75	6	8.0
Blood (less than 1,000 cc.).....	47	4	8.5
None.....	90	5	5.5

\* It is difficult to appraise the value of transfusions by statistical means. Individual case histories make it evident that whole blood and plasma were invaluable in combating shock and restoring blood volume.

In the original Meulengracht diet, iron medication and antacid-antispasmodic agents supplement the diet. In the present series aluminum hydroxide has been the recent antacid of choice. In table 6 the 45 patients who were treated under the antacid regimen usually had an initial period of starvation prior to the onset of a Sippy or soft diet.

An observer in Meulengracht's clinic has been quoted as saying: "The patient is urged to wipe the blood off his lips and eat a beef-steak." The value of this advice given more than ten years ago in the light of our present knowledge of protein requirements and hypoproteinemia is almost prophetic.

Transfusion: More than 50 per cent of the 218 patients in this series (table 7) received either blood or plasma transfusions. The amount of the transfusion varied from a single unit of 250 cc. to thirty-

four transfusions of 500 cc. or more of whole blood each received by a patient during the course of a single stay in the hospital. This patient subsequently underwent a subdiaphragmatic vagotomy in conjunction with a subtotal gastric resection and has had no further hemorrhage (six months after his discharge from the hospital). In this case transfusion must be surely considered the sole factor responsible for the preservation of life during the course of active hemorrhage from an ulcer.

The medical literature seems almost completely in disaccord regarding the pros and cons of transfusion as a procedure of choice in the treatment of hemorrhage from an ulcer. Those opposed to transfusion cite the statistics of Christiansen and Cullinan and Price showing an increased mortality rate following its use. On the other hand, Gordon-Taylor, in his enthusiasm, quotes Bennett as saying that "blood transfusion correctly applied is the most important single factor in saving life in gastro-duodenal hemorrhage."

From the present statistics it is difficult to appraise the value of transfusion or predicate its salutary effect on the mortality rate, for transfusions were used chiefly in the more seriously ill patients. However, from a review of the individual case histories one is impressed by the fact that whole blood and plasma were almost invaluable in combating shock and restoring normal blood volume in a number of patients seriously ill from hemorrhage.

**Antacids and Other Methods of Medical Treatment:** Over the course of the years spanned by this study the patients at the Johns Hopkins Hospital have received both soluble and nonabsorbable antacids. The former are represented by the salts of sodium, calcium, bismuth and magnesium and are used chiefly in the Sippy and related rituals. The nonabsorbable antacids are mainly those represented by colloidal aluminum hydroxide.

Other methods of treatment, such as the oral administration of mucin or the hyperalimentation of amino acids or hydrolyzed proteins as suggested by Co Tui were not routinely used at this hospital. Treatment by continuous intragastric drip, the insufflation of powdered posterior pituitary injection, high voltage roentgen therapy, the administration of vitamins C or K or of newer preparations such as enterogastrone, anthelone or the powdered plastic amberlite, the use of oxalic acid as a powerful blood coagulant and the ingestion of hemostatic sponges all have their proponents in the medical press, but none of these methods received a therapeutic trial in this series of cases of bleeding peptic ulcer.

**Surgical Treatment.**—Regardless of the perseverance of certain internists in conservative medical management of hemorrhage from an ulcer, it is a positive fact that a minimum of 5 or 10 per cent of patients



so treated die. Heuer expressed the belief that the prospects are even grimmer and stated that "approximately 15 per cent of patients who enter the hospital with massive hemorrhage die unless they can be saved by prompt surgery." Other distinguished surgeons, such as Wangersteen and Allen in this country and Gordon-Taylor and Finsterer abroad, have stated the opinion that some of these lives may be salvaged by early surgical treatment. The *British Medical Journal*, however, indicated its opinion of prompt surgical intervention during active hemorrhage from ulcer by saying:

The subject is a debatable one, but in the absence of any really trustworthy guide to prognosis at an early stage (after which the information becomes less and less valuable) most surgeons are likely to maintain the attitude that it is not justifiable to endanger the safety of many in the hope of saving a few.

The clinical problem of the surgical care of hemorrhage from an ulcer thus resolves itself into (1) the differentiation, if possible, of cases which cannot be controlled without surgical treatment, (2) the selection

TABLE 8.—*Surgical Treatment of Bleeding Ulcer at the Johns Hopkins Hospital*

Time of operation following initial onset of bleeding	Number
1. Immediate (operation within first 48 hours).....	3
2. Early (operation 3rd to 8th day).....	12
3. Late (operation after 8th day with continued bleeding).....	25
4. Late (operation after 8th day without continued bleeding).....	42
Source of bleeding removed at operation	
1. Yes.....	33
2. No.....	49
Recurrence after operation as noted in hospital record	
1. Yes.....	12
2. No.....	12
3. Unknown.....	58

of an optimum time for operation and (3) the determination of which type of operation will best control the source of bleeding, save the greatest number of lives and prevent further recurrent hemorrhage. It is beyond the scope of this paper to attempt to discuss in detail the many varied solutions which have been put forth. Suffice it to say, however, that with the present limited means of prognosis there is no way of telling which cases will prove fatal if unchecked by surgical measures. Of all the criteria assembled to differentiate those who will succumb without the unctions of surgical treatment, perhaps failure of hemorrhage to stop during a medical regimen (including transfusions and prompt feeding) is the most indicative. This, of course, requires a certain time lag during which the optimal periods for early surgical intervention will have passed—the so-called golden forty-eight hours of Finsterer.

Surgical treatment of hemorrhage due to ulcer at the Johns Hopkins Hospital (table 8) has consisted for the most part of conservative management during the phase of active bleeding. Partial gastric resec-

tion (table 9) was the operation of choice in 56 patients of a total of 82 receiving surgical treatment. However, early operation in the midst of hemorrhage as suggested by Finsterer, Gordon-Taylor, Heuer, Allen and Wangenstein was infrequently performed. Late operation, usually carried out when bleeding had ceased or at least decreased its tempo, was performed in 82 per cent of the patients.

By a careful scrutiny of the operative records, the pathologic reports and the findings at autopsy, it was noted that in only 40 per cent of the operative cases was the source of bleeding actually removed by operative means. What spell of the surgical procedure caused the bleeding to cease in the remainder of the cases, in which the ulcer was left in situ, remains open to speculation. However, the hemostatic effects may be more apparent than real, for in the majority of these cases surgical intervention was delayed until the bleeding had already stopped of its own accord.

TABLE 9.—*Surgical Treatment* \*

	Number	Deaths	Per Cent Mortality
Gastric resection, partial.....	56	4	7.1
Gastric resection, complete.....	0	0	0
Gastroenterostomy with excision of ulcer.....	7	0	0
Gastroenterostomy without excision of ulcer...	6	0	0
Gastroduodenostomy .....	2	0	0
Vagotomy plus additional procedures.....	7	0	0
Miscellaneous procedures.....	4	0	0
Total.....	82	4	4.9

\* The exceptionally low surgical mortality rate must be considered in the light of the somewhat higher medical mortality rate. Under a conservative surgical regimen patients considered to have severe hemorrhage are frequently too ill to undergo operation.

Follow-up notes and readmission records were available for only about one third of the patients receiving surgical treatment. A review of this limited number of follow-up cases reveals that a recurrence of hemorrhage was present about as often as not after ventriculus operations. The type of operation appeared to have little bearing on the recurrence rate. In fact the source of hemorrhage was presumed to have been removed in 7 of the 12 patients in whom hemorrhage recurred after operation.

Seven patients were subjected to vagotomy in addition to some ancillary operative procedure on the stomach, and after six months of careful follow-up study none of these had had a recurrent hemorrhage due to ulcer. This confirms a personal communication from Dragstedt in which he stated that vagotomy alone sufficed as a sovereign remedy for 34 of 35 cases of severe hemorrhage due to ulcer. No deaths

occurred, and there were no recurrences of hemorrhage in his series, although the period of follow-up was not stated.

#### MORBID ANATOMY

In this series there were 16 fatal cases, an over-all mortality rate of 7.3 per cent. Permission to perform an autopsy was granted in 14 of these 16 cases. In almost all the gross specimens at autopsy it was possible to demonstrate an eroded artery on the posterior wall of the duodenum or along the lesser curvature of the stomach. Bleeding ulcers astride the lesser curvature of the stomach had usually eroded into one of the major branches of the right or left gastric arteries, whereas the deep penetrating ulcers of the posterior duodenum were in the neighborhood of the pancreaticoduodenal artery and had caused necrosis of its vessel wall.

TABLE 10.—*Mortality from Medical Treatment*

	No. of Cases	Deaths	
		Number	Per Cent
Crohn, B. B.....	94	4	4.2
Altken, R. S.....	234	20	8.5
Meulengracht, E. ....	365	5	1.3
Witts, L. J.....	20	0	0
Kirsner, J. B. and Palmer, W. L.....	230	7	3.1
Heuer, G. J.....	306	18	5.8
Rasberry, E. A., Jr. and Miller, G. T. (collected cases)...	2,111	55	4.0
Johns Hopkins Hospital.....	136	12	8.8
Total.....	3,490	151	4.3

#### COLLECTED STATISTICS

Data collected from the literature are difficult to appraise because they are not always clear as to the exact type of medical regimen instituted or the precise severity of the hemorrhage due to ulcer which the authors are analyzing. Complementary therapeutic procedures such as the use of transfusions, sedatives, fluids and antacids all tend to muddle the reckoning and garble the statistics. There is substantial evidence, however, to support the contention of Andresen and Meulengracht, among others (table 10), favoring prompt and frequent feeding regardless of whether a gelatin, Sippy or high protein diet be used. However, if this be the procedure of choice, surgical treatment must wait. It could be undertaken only after a few days of a conservative therapeutic trial of medical management and notwithstanding the fact that hemorrhage from ulcer has been persistent and perhaps profuse. Under such adverse conditions the operative mortality necessarily may be high, but possibly a few additional lives may be salvaged.

The fact that at this hospital the mortality of patients treated medically was 8.8 per cent among patients on a conservative regimen may be interpreted as meaning that most patients with profound exsanguination were kept on medical therapy and not subjected to surgical treatment despite their precarious condition.

The mortality from hemorrhage due to ulcer at a few of the leading surgical clinics throughout the world (table 11) reveals a wide range of death's roll call. Finsterer advocated immediate surgical intervention within the early stages of active hemorrhage. The mortality in his skilful hands was only 5.9 per cent. In the period between 1933 and 1939 Gordon-Taylor found an operative mortality of 5.5 per cent among personal cases in which he operated early. Patients who were operated on late had a fatality rate of 36 per cent. At the Johns Hopkins Hos-

TABLE 11.—*Mortality from Surgical Treatment*

	No. of Cases	Deaths	
		Number	Per Cent
Crohn, B. B.....	7	5	71.4
Ross, K. ....	43	26	60.4
Aitken, R. S.....	21	7	33.3
Finsterer, H. ....	51	3	5.9
Allen, A. W.....	144	21	14.6
Heuer, G. J.....	31	9	29.0
Gordon-Taylor, G. ....	71	13	18.3
Wangensteen, O. H.....	10	2	20.0
Johns Hopkins Hospital.....	82	4	4.9
Total.....	460	90	19.5

pital the patients were for the most part operated on late; the mortality rate of 4.9 per cent is a creditable record regardless of the favorable cases chosen.

#### SUMMARY

A study of 218 cases of bleeding peptic ulcer is presented. All patients in this series had gross hemorrhage due to ulcer and were treated as bed patients at the Johns Hopkins Hospital.

The statistics of this group of cases were analyzed according to yearly and monthly incidence and race and sex ratios. The morbidity was reviewed as related to age, loss of blood, arteriosclerosis, gastric retention, azotemia, intractable pain, number of episodes of bleeding and history of ulcer. The selection of patients whose hemorrhage is likely to prove fatal if not surgically checked as contrasted with those whose hemorrhage is likely to cease spontaneously remains primarily a problem of clinical judgment.

All aspects of the medical treatment of hemorrhage from ulcer are considered, and the value of a prompt and frequent feeding program is

emphasized. A modified Meulengracht regimen combined with antacids and transfusions resulted in no deaths in 76 cases.

The surgical treatment of 82 patients with bleeding ulcer is analyzed with respect to time of operation, surgical procedure, operative attack on the source of bleeding and recurrence rate. The value of vagotomy in 7 patients with hemorrhage due to ulcer is discussed.

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## EFFECT OF APPLICATION OF SEVERAL ANTIBACTERIAL SUBSTANCES ON HEALING OF WOUNDS

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DETROIT

IN SEVERAL previous communications from this laboratory,<sup>1</sup> there have been presented the results of simple animal experiments to determine the effect of the topical application of various agents on the healing of wounds. We have observed the healing of two symmetric cutaneous defects on the abdominal wall of the guinea pig; one of these wounds was treated with the test substance while the other served as a control. This type of experiment appears to be a reliable indicator of the response which may be expected from human tissue. For example, a number of substances recommended for the treatment of burns were tested.<sup>1b</sup> Among these was tannic acid, which produced a conspicuous delay in healing. This experimental finding has had ample clinical confirmation. Many other agents have failed to show the stimulating effect claimed by their sponsors. This paper presents the results of experiments on wound healing with five antibacterial substances which have been used more or less extensively in local treatment: sulfanilamide, sulfathiazole, sulfadiazine, penicillin and nitrofurazone (furacin,<sup>®</sup> 5-nitro-2-furaldehyde semicarbazone).

Although the sulfonamide compounds have been employed widely, there are surprisingly few reports of controlled healing experiments with them. Bricker and Graham<sup>2</sup> stated that they could detect an inhibitory effect on the tensile strength of healing stomach wounds when their dogs were fed 3 Gm. of sulfanilamide daily. Taffel and Harvey<sup>3</sup> carried out

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similar experiments with rats but did not note a similar effect. Smith and Livingston,<sup>4</sup> using a variety of animals, found delay in healing of 60 per cent of the wounds treated with sulfanilamide powder. With sulfathiazole and sulfadiazine, the delay in healing was observed in 50 and 40 per cent of the animals, respectively.

A controlled clinical study was carried out by Bick,<sup>5</sup> who placed sulfonamide drugs in 50 clean operative wounds and compared the healing with that of 50 controls. He found that healing was retarded at least 50 per cent and that there was excessive cutaneous scarring. A diametrically opposed opinion was expressed by Key,<sup>6</sup> who implanted the drugs in more than 600 operative wounds. The local complications in this series included 7 hematomas, 1 separation of wound margins, 2 stitch abscesses and 2 infections. It was thought that the remaining wounds healed in a normal manner without excessive scar formation and that the average period of hospitalization was shortened by the use of the drugs.

Posch, Maun, Pilling and Hirshfeld<sup>7</sup> put sulfanilamide and sulfathiazole crystals into the subcutaneous tissues of human volunteers and removed the entire wounds for microscopic study after varying intervals of time. They concluded:

From a study of the excised biopsy specimens it is evident that sulfanilamide and sulfathiazole act as irritants to the dermis and the subcutis. In addition, they may produce necrosis and marked leucocytic response in adjacent tissues. However, the deleterious effects are short-lived and are not evident in wounds 7 to 10 days old.

Studies of the Subcommittee on Surgical Infections of the National Research Council, published by Meleney,<sup>8</sup> indicated that the sulfonamide compounds did not lessen the incidence of local infection in contaminated wounds, compound fractures or burns.

Howes<sup>9</sup> reported the toxicity of a number of antibacterial substances for tissue cultures of epithelial cells. Benzalkonium chloride (zephiran

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chloride<sup>®</sup>), P-chlorophenol and tyrothricin in the dilutions employed to inhibit the growth of bacteria were toxic to the cells. Penicillin calcium was inert, while streptomycin and sulfamylon<sup>®</sup> (para-[aminomethyl]-benzene sulfonamide) were mildly inhibitory. Wound-healing studies on nitrofurazone were carried out by Dodd, Hartmann and Ward.<sup>10</sup> They found that it did not delay the healing process in rabbits.

#### PRESENT STUDY

*Method.*—The guinea pig was anesthetized with ether, and the abdomen was shaved and prepared with an antiseptic solution (hexylchloro-m-cresol). Symmetric circular or ovoid cutaneous defects were made on each side of the midline (fig. 1). The wound on the animal's left served as the test wound, and the other

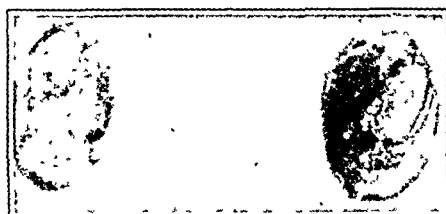


Fig. 1.—Freshly made cutaneous wounds on the abdominal wall of a guinea pig.

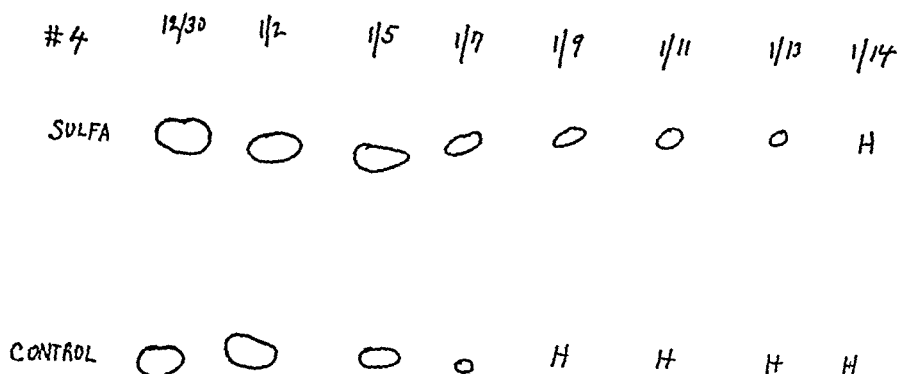


Fig. 2.—Tracings showing progress of a typical experiment (application of sulfanilamide crystals to a test wound).

was the control. After recording the original size of the wounds by tracing the outlines on sterile cellophane, we applied the test substance to the appropriate wound. The control wound was covered with petrolatum gauze. Ordinary gauze squares completed the dressing on both wounds. The dressing was held in place by a 3 inch (7.61 cm.) wide strip of adhesive tape passed around the animal's body. The wounds were measured every two days, at which time more of the test substance was applied. Each agent was used on 12 animals.

10. Dodd, M. C.; Hartmann, F. W., and Ward, W. C.: The Local Application of Nitrofurazone Compounds with Special Reference to Use on Wounds, Surg., Gynec. & Obst. 83:73, 1946.

The sulfonamide compounds were used in the form of sterile, dry crystals. The wounds were liberally frosted. The penicillin was in the form of an oxy-cholesterol-petrolatum ointment base (aquaphor®) containing 1,000 Oxford units per gram. The nitrofurazone (furacin®) was in a base consisting of carbowax 1540,<sup>11</sup> carbowax 4000® and polyethylene glycol (furacin-soluble dressing®).

*Results.*—Figure 2 is a sample of the type of permanent record made by transferring the cellophane tracings to white paper. Results of a

TABLE 1.—*Effect of Sulfanilamide Crystals on Experimental Wound Healing*

Animal No.	Days Required for Healing		Effect on Healing*
	Control Wound	Test Wound	
1.....	13	15	Delayed
2.....	11	16	Delayed
3.....	11	15	Delayed
4.....	11	16	Delayed
5.....	Died seventh day		..
6.....	Died fifth day		..
7.....	11	13	Delayed
8.....	11	13	Delayed
9.....	11	13	Delayed
10.....	13	14	Delayed
11.....	15	16	Delayed
12.....	15	15	No effect

\* Healing was delayed in 9 of the 10 animals which survived. The cause of death of 2 animals is not known.

TABLE 2.—*Effect of Nitrofurazone (Furacin®) on Wound Healing*

Animal No.	Days Required for Healing		Effect on Healing*
	Control Wound	Test Wound	
1.....	12	14	Delayed
2.....	12	10	Hastened
3.....	10	10	No effect
4.....	12	12	No effect
5.....	10	10	No effect
6.....	13	12	Hastened
7.....	10	10	No effect
8.....	12	13	Delayed
9.....	17	14	Hastened
10.....	12	12	No effect
11.....	12	12	No effect
12.....	14	14	No effect

\* The drug had no effect in 7 animals, delayed healing in 2 animals and accelerated healing in 3 animals.

typical experiment, consisting in the application of sulfanilamide crystals to wounds on 12 animals, are represented in table 1. It is seen that in no instance did the wound treated with the crystals do better than the control, and in 9 of the 10 animals which survived there was delay in

11. Carbowax compounds are polyethylene glycols of high molecular weight.

healing on the treated side. From these facts it is concluded that the drug is inhibitory, and this effect is indicated in the conclusions in table 3. The data on another typical experiment are presented in table 2. It is evident that there was no significant acceleration or delay in wound healing as a result of the application of nitrofurazone (fig. 3).

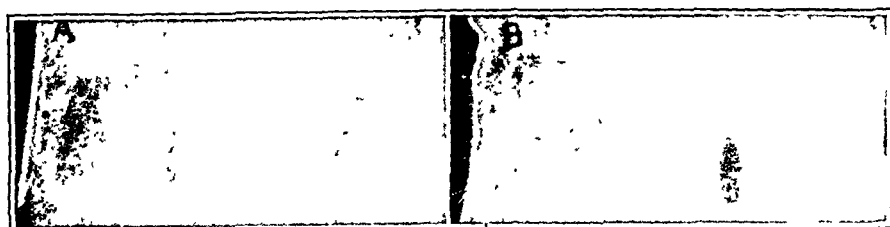


Fig. 3.—Wounds on 2 animals from the sulfadiazine series. (A) Both wounds healed on the eleventh day. (B) The control wound healed; the wound treated with sulfadiazine did not heal until four days later.

TABLE 3.—*Summary of Experiments on Effect of Five Antibacterial Substances on Wound Healing*

Substance Tested	Healing Hastened	No Effect	Healing Delayed	Conclusions of Effect on Healing
Sulfanllamide.....	0	1	9	Delays
Sulfathiazole.....	2	3	7	Delays
Sulfadiazine.....	3	7	2	No effect
Penicillin.....	3	6	3	No effect
Nitrofurazone ("furacin").....	3	7	2	No effect

#### SUMMARY

Five antibacterial substances were placed on uninfected wounds in guinea pigs to determine the effect on the rate of healing. Sulfanilamide and sulfathiazole crystals caused delay in healing. The wounds dressed with sulfadiazine, penicillin ointment and nitrofurazone (furacin®) healed in the same time as did the controls.

## COSTOCLAVICULAR COMPRESSION

Relation to the Scalenus Anticus and Cervical Rib Syndromes

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THIS study includes a series of cases in which the subclavian artery and brachial plexus were compressed between the clavicle and the first rib. In a previous paper<sup>1</sup> a series of 9 cases of cervical rib were reported, in 5 of which costoclavicular compression of the neurovascular structures leading to the arm was the outstanding feature. In the present series of 14 cases a cervical rib was actually present in only 2. In the remaining 12 the compression was between the clavicle and the first thoracic rib. The condition is characterized by vascular and neurologic symptoms together or separately. The pulse to the arm is markedly reduced in volume or shut off entirely when the shoulders are thrown back as in the attention position.

On reviewing the literature, one finds many theories formulated in an attempt to explain the mechanism producing symptoms in the so-called scalenus anticus and cervical rib syndromes. Yet these theories do not explain adequately the circulatory disturbances often found. The scalenus anticus muscle as an instrument of counterpressure has enjoyed considerable popularity.<sup>2</sup> Irritation of abnormally placed sympathetic nerve fibers as they cross a cervical or first thoracic rib has been considered a factor in vasospasm.<sup>3</sup> The clavicle, except in a few recent

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contributions, has not been given the place it warrants as a factor of counterpressure in these compression syndromes.<sup>4</sup>

Adson and Coffey<sup>2</sup> in 1928 attempted to show that symptoms occurring in cases of cervical rib were often due to pressure from the scalenus anticus muscle. They claimed relief of symptoms by scaleniotomy without removal of the anomalous rib. They devised a test later referred to as the Adson maneuver which was believed to indicate whether or not the scalenus anticus muscle was producing neurovascular compression in a case of a cervical rib. This test consists of turning the head to the side of the lesion, hyperextending the neck and taking a deep breath. The scalenus anticus muscle presumably would then be put under sufficient tension to compress the subclavian artery decreasing or shutting off the pulse to the arm. Actually, the scalenus anticus muscle itself should not increase in tension on the affected side in this maneuver but should reciprocally relax unless it happened to be the site of fibrosis, as will be seen later is frequently the case.

Ochsner, Gage and DeBakey<sup>5</sup> reported a series of cases without cervical rib in which they believed abnormal compression to the neurovascular structures passing to the arm was produced by the scalenus anticus muscle. In these cases they found a fibrositis of the offending muscle. They believed that the fibrositis led to spasm of the muscle elevating the first rib, which resulted in compression and stretching of the large nerve trunks. It was their belief that this condition frequently occurred in persons in whom the shoulder descended to an abnormally low level. Actually, compression symptoms from the descent of the shoulder would not be expected to be produced by the scalenus anticus muscle, which is not attached to the shoulder girdle. It is highly probable that the compression of the subclavian artery in the Adson maneuver and the fibrosis of the scalenus anticus as found by Ochsner were often both due to pressure from the clavicle.

Craig and Knepper<sup>6</sup> suggested that scaleniotomy alone is not sufficient in many cases and recommended the removal of the cervical rib in addition.

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Telford,<sup>3c</sup> Todd,<sup>3d</sup> Jones<sup>3b</sup> and Blair<sup>3a</sup> believed that the circulatory disturbances associated with cervical rib syndrome were due to irritation of the sympathetic nerve fibers as they passed over the anomalous rib.

Neither the scalene compression theory nor the theory of irritation of the sympathetic nerve fibers adequately explains many factors, among which are (1) the frequent occurrence of an aneurysm in the subclavian artery just beyond the scalenus anticus muscle and (2) embolic phenomena which may occlude any of the smaller peripheral arteries singly. These conditions are best explained on the basis of costoclavicular compression.

Falconer and Weddell<sup>4b</sup> reported 3 cases in which the subclavian artery was compressed between the clavicle and the first thoracic rib. In these cases the pulse was obliterated when the shoulders were thrown down and back. They were able to demonstrate compression of the subclavian artery between the clavicle and the first rib on the operating table before and after scaleniotomy. In the same case they were able to demonstrate absence of scalene compression by the Adson maneuver performed at the operating table with the scalenus anticus muscle exposed. They tested 100 apparently normal persons by having them throw the shoulders down and back and found that the pulse was reduced in volume in 54 cases. They must have caused their subjects to force the shoulders down and back to a considerable degree because in a larger series of apparently normal persons we were not able to cause the same degree of pulse occlusion as in the cases presenting costoclavicular compression symptoms.

Among others who recognized the importance of the clavicle in these compression syndromes are Walshe and Wayburn-Mason.<sup>4c</sup> It was their impression also that the compression symptoms are due to the pressure between the clavicle and the first thoracic or cervical rib. The findings reported in this paper are in agreement with the observations of the authors who state: "The clavicle and first rib act like the two arms of a vise in which the intervening structures are recurrently compressed."

This theory does not exclude the role of the first thoracic rib in traction, stretching and angulation. The damage to the artery as a result of excessive exercising leads to thrombosis in the wall. Thrombi are then broken off and produce emboli in smaller vessels, leading to ischemia and even gangrene. Intermittent compression involves the arteries, muscles and nerves. The cause of the symptoms is related to (1) the respiratory excursions of the thoracic cage which occurs 23,000 times in twenty-four hours and (2) the movements of the shoulder. The recurrent friction, stretching and compression sets up an inflammatory reaction around the structures between the rib and the clavicle.

Stretching alone may affect the lower trunk of the brachial plexus, producing symptoms referable to the ulnar nerve.

One of the cases which one of us (McGowan) previously reported<sup>1</sup> presented a picture similar to that just mentioned. The patient had thrombosis in the right radial and ulnar arteries, with beginning gangrene in three fingers. It was found that his brachial pulse was obliterated when he threw the shoulders back as in the position of attention. This occlusion was found to be between the clavicle and a cervical rib and was not related to the scalenus anticus muscle. Proof of this was furnished by the fact that the pulse could be felt in the posterior triangle of the neck beyond the scalenus anticus muscle at the same time that it could not be felt in the brachial artery. In 3 cases previously reported in this same paper in which the pulse was occluded in the attention position, a process of fibrosis involving the muscles, arteries and nerves was found at operation.

Hansson<sup>7</sup> has recommended exercises in cases of scalenus anticus syndrome aimed at elevation of the shoulder girdle by strengthening the trapezius and levator scapulae muscles. Favorable results reported from such exercises are an indication that the clavicle must have been the important factor of counterpressure since elevation of the shoulder would not have affected the scalenus anticus muscle.

Judovich and others<sup>8</sup> and Aynesworth<sup>4a</sup> have separately mentioned the importance of narrowing of the costoclavicular space in cervical rib and scalenus anticus syndromes.

#### CLINICAL ASPECTS

The important etiologic factor in this compression syndrome is, therefore, a narrowing of the space between the clavicle and the first thoracic or cervical rib. The structures in this costoclavicular space, as previously mentioned, are compressed by a vise, one arm of which is formed by the clavicle and the other by the first rib. This is part of the price which some human beings must pay for the privilege of walking in the upright position, for if man walked on all fours or swung from a tree, the clavicle would be thrust forward, leaving an adequate costoclavicular space for the arterial and nerve trunks to pass to the extremity concerned.

A factor leading to the narrowing of the costoclavicular space may be abnormal descent of the shoulder girdle such as occurs in persons with muscular weakness, particularly in the aged. It may also occur in a soldier from carrying a pack or a rifle. A second factor which narrows

7. Hansson, K. G.: Scalenus Anticus Syndrome, *S. Clin. North America* **22**:611-620 (April) 1942.

8. Judovich, B.; Bates, W., and Drayton, W., Jr.: Pain in the Shoulder and Upper Extremity Due to Scalenus Anticus Syndrome, *Am. J. Surg.* **63**:377-381 (March) 1944.



the costoclavicular space is the abnormal elevation of the first rib. This may be brought about by excessive use of the muscles of extraordinary respiration, particularly those of the scalene group, such as occurs in vigorous exercises associated with basic military training or in persons suffering from emphysema. The intermittent compression sets up an aseptic inflammatory reaction leading to fibrosis involving the scalenus anticus muscle, the subclavian artery and the trunks of the brachial plexus. This reaction may spread to involve even the stellate ganglions, gradually producing a sympathetic disturbance which is irritative at first and leads to vascular spasm and later is paralytic and results in Horner's syndrome.<sup>4c</sup>

Symptoms may be neurologic or vascular or both. Neurologic symptoms consist of pain in the scapular region radiating up the back of the neck and down the arm. This pain is of a lancinating character and may be aggravated by depression of the shoulder, pressure lateral to the scalenus anticus muscle or abnormal positions such as that of the Adson maneuver or the position of attention.

Physical examination may reveal paresthesia or anesthesia of the area supplied by the ulna nerve, although frequently the median nerve may be involved. Trophic disturbances such as muscular atrophy, absence of hair, weakness of the grip or deformities of the nails may occur.

The vascular symptoms are manifested by numbness of the extremities and pallor coming on during periods of downward and backward depression of the shoulders such as occurs in carrying a pack or rifle or in standing at attention for a long period.

Diagnosis is made by having the patient throw the shoulders down and back as in the attention position. The pulse will be reduced in volume or completely obliterated. A positive reaction to the Adson maneuver indicates that the scalenus anticus muscle is the seat of fibrosis and division of this muscle should result in a cure.

Treatment consists of exercises aimed at strengthening the trapezius and levator scapulae muscles, and so producing elevation of the shoulder. The patient is instructed not to throw his shoulders back in assuming the position of attention but to allow them to hang freely or even to drop slightly forward. Removal of a part of the first rib has been done by Falconer and Weddell. Removal of the clavicle has not been performed for this condition but has been done with impunity for other conditions and without weakening the shoulder girdle. It seems that removal of the middle third of the clavicle might be beneficial in severe cases not responding to exercises.

#### METHOD OF STUDY AND FINDINGS

One hundred and twenty-nine persons were studied with reference to this syndrome. Of these, 108 were supposedly normal recruits who were checked during their routine physical examination for officer candi-

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date school. These showed no abnormal symptoms. The remaining 21 presented themselves with symptoms referable to the arm simulating the scalenus anticus or cervical rib syndrome. Of these, 14 were definitely found to have costoclavicular compression. The symptoms were either vascular or neurologic. The vascular symptoms included swelling in the arm, numbness of the arm when at the attention position especially while wearing a heavy overcoat, numbness while driving a truck or carrying a pack, pallor and coldness of the extremity. The neurologic symptoms complained of included muscle weakness in the hand and arm, pain in the shoulder, a tingling sensation, muscle atrophy, pain over the scapula radiating down the medial aspect of the arm aggravated by pressure over the scalenus anticus, pain in the pectoral region aggravated by turning the head, tingling, hyperesthesia, pain in the scapular region radiating up the back of the neck and numbness in the arm following weight bearing. Blood pressure determinations were made on each arm with the patient standing, under the following conditions: (1) with the shoulders in the normal forward position; (2) with the head turned toward the affected side and hyperextended as in the Adson maneuver, and (3) with the shoulders pressed down and back in the attention position.

Of the 14 patients with costoclavicular compression, 7 had symptoms on the right side, 5 had symptoms on the left and 2 had symptoms on both sides. Eleven of these men were right handed, and 3 were left handed so far as writing was concerned; however, 3 right-handed patients preferred to use the left arm for most weight-bearing tasks but had been taught to use the right hand in school. Of the 6 actually left-handed persons, 5 had symptoms on that side. The sixth left-handed person preferred to use the left arm because of muscular weakness in the right, which arm remained asymptomatic until he was obliged to use it to carry a rifle or a pack. In general, therefore, symptoms occurred in the arm that was the most frequently used for weight bearing in every case except in the one in which there was muscular weakness on the opposite side. In most cases the shoulder on the symptomatic side was lower than that on the other side. In 3 cases this shoulder was lower because of faulty posture (fig. 1A).

The attention position produced a reduction or obliteration of the pulse on the affected side in all 14 cases and a complete obliteration of the pulse in 10 of those cases. This test is carried out in the following manner: A blood pressure cuff is placed around the upper part of the arm with the patient in a standing position. The shoulder is held well forward and upward and the blood pressure is recorded. The patient is then asked to put the shoulders down and back approximately in the position adopted by a soldier at attention. The blood pressure readings are again taken. The reaction to the test is considered positive when

there is a reduction of blood pressure of 20 points or more. In the 4 patients with incomplete obliteration of pulse the attention position resulted in a reduction of blood pressure ranging from 25 to 75 mm. of mercury. In only 3 cases were there positive findings on the unaffected side, and in these they were more pronounced on the affected side. In only 1 case was the pulse reduced equally on both sides, and in that case symptoms were bilateral. The reaction to the attention position test as an index of costoclavicular compression was found to be 100 per cent in agreement with the symptoms.

With the Adson maneuver the findings were less specific. This maneuver is carried out as follows: The blood pressure cuff is placed on

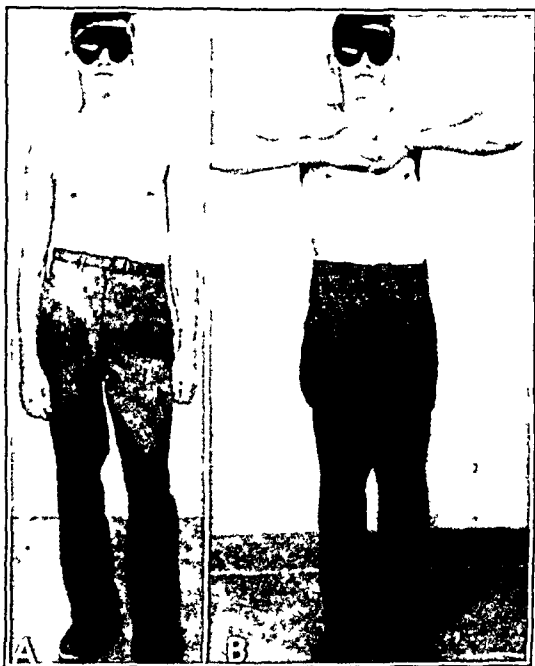


Fig. 1.—*A*, a case of costoclavicular compression from faulty posture. This is the position the man had adopted in standing before entering the army. Note the low level of the right shoulder. *B*, note the leveling effect on the shoulders of the first phase in corrective exercises. The second phase consists of bringing the hands over the head clasped in this manner.

the arm, the shoulder is placed forward and upward and the blood pressure is recorded. With the shoulder still in the forward position, the head is turned to the side being studied, and the patient is then asked to throw the head back, look up to the ceiling and take a deep breath. The reaction to the test is considered positive if there is a reduction in systolic blood pressure of 20 points or more. A positive reaction indicates fibrosis in the scalenus anticus muscle. The reaction was positive in 9 cases of the 14. The pulse was completely obliterated in only 1 case, as against 10 in the attention position test. Among the 9 cases in which the test

gave a positive reaction, vascular compression was present on both sides in 4 cases and on the affected side alone in only 5 cases. In the 14 cases studied, the Adson maneuver elicited a specifically positive reaction in only 5. There were 5 cases in which the Adson maneuver elicited a negative reaction and the attention position a positive reaction. There were 3 cases in which the Adson maneuver gave a false positive reaction, that is, when the patient assumed the position for the maneuver, he automatically pushed the shoulder down and back, so reducing the pulse volume by costoclavicular rather than by scalene compression. When the test was repeated with the shoulder kept in a forward position, the reaction was found to be negative. It is probable that many patients in the past reported as reacting positively to the Adson maneuver and with a diagnosis of the scalenus anticus syndrome, and indeed frequently operated on, actually suffered from costoclavicular compression.

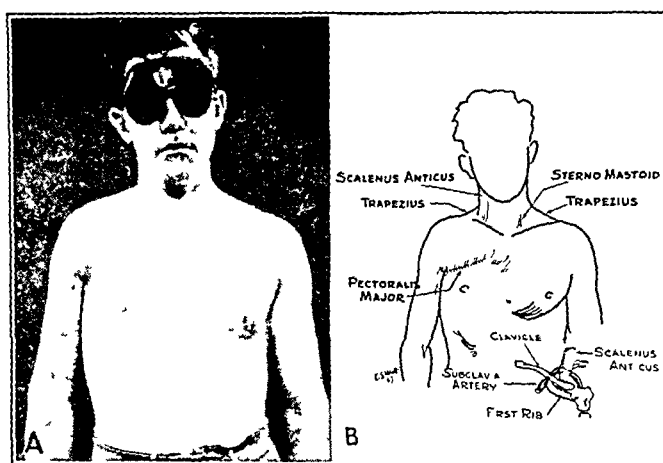


Fig. 2.—*A*, a case of costoclavicular compression as a result of lack of support to the shoulder girdle because of muscle weakness and dorsal scoliosis which elevates the first rib toward the clavicle. Note atrophy of the right major pectoral and trapezius muscles. The shoulder was supported only by the levator scapulae muscle. Note also the lack of prominence of the sternomastoid muscle on the right. The scalenus anticus muscle is unusually prominent (compensatory hypertrophy), producing further elevation of the first rib. The shoulder is held in an elevated position in order to avoid costoclavicular compression. However, 30 pounds (13.6 Kg.) of pressure on the tip of the shoulder was sufficient to depress it to the point at which the pulse was occluded. *B*, a diagrammatic key to *A*.

The ages of the 14 patients were 18 to 42 years. The length of service was less than four months in all but 3 cases. The short duration of service is explained partially by the fact that patients were drawn from an infantry replacement training center, where the period of training did not exceed three months in many cases. The 3 patients in the older age group could be explained on the basis of a weakening of the trapezius muscle resulting in a drop of the shoulder girdle. One of these patients had been in the tropics for thirty-four months, where general muscular atony had developed. The other 2 had had sedentary occupations in the army and

had suddenly been transferred to an actively training unit. Symptoms before induction were present in 7 cases, 50 per cent. The condition could have been picked up in the remaining 7 during the course of the induction examination by simply having each man throw the shoulders back at attention while the radial pulse was being palpated by the examiner.

#### TREATMENT

All patients were treated by having them placed on limited duty, with avoidance of weight bearing or carrying a pack or a rifle. They were instructed not to throw their shoulders down and back during the attention position but to allow them to remain slightly forward. They were instructed in exercises aimed at strengthening the trapezius and levator scapulae muscles (fig. 1*B*). The results could be evaluated properly in only 4 cases which could be followed, and in these improvement was striking. The remaining men probably were improved, because they usually returned fairly promptly from their units if they continued to have symptoms. The training in this particular camp was at a fast tempo, and men were rapidly returned to the hospital if they were unable to keep up the pace.

#### CONTROL STUDY

In order to evaluate the accuracy of the present findings 108 apparently normal persons were studied. These were taken from a group of men during the routine examination for admission to officer candidate school. The tests were performed before the man was questioned concerning any symptoms referable to the arm. The following tests were conducted: (1) Adson maneuver; (2) the attention position of the shoulders; (3) extreme backward and downward shoulder compression (exaggerated attention position), and (4) roentgen study for evidence of cervical rib.

The findings showed 88 patients in whom the reactions to all tests were entirely negative and who had no subjective symptoms; 16 patients showed a diminution of the pulse to the arm, particularly in the exaggerated attention position but not a complete absence of pulse beat. All these 16 men had hypertrophy of the neck musculature, but there were no subjective symptoms. The decrease of pulse beat in these 16 cases we do not consider abnormal. They correspond to the cases reported by Falconer and Weddell, who found forceful decrease in pulse volume in downward and backward shoulder compression. The remaining 4 of the 108 controls showed definite evidence of abnormality.

The first of these 4 patients presented an absence of pulse in the "position of attention," with a negative reaction to the Adson maneuver. This man had symptoms consisting of a tingling sensation and numbness in the hands while at attention and when carrying a pack. Roentgenologic examination showed bilateral cervical rib. The second patient

presented a diminution of pulse beat on both sides while in the attention position and an absence of pulse in the extreme attention position but a negative reaction to the Adson maneuver. He had no subjective symptoms except for occasional numbness of short duration. The third patient presented a positive reaction to the Adson maneuver on both sides. The radial pulse at attention position and extreme attention position was also obliterated bilaterally. This man had no subjective symptoms in spite of the fact that he had completed thirteen weeks of basic training. Roentgenologic study did not reveal a cervical rib. The fourth patient reacted negatively to all compression tests but showed bilateral cervical rib on roentgen examination. These were too short to produce symptoms.

In summary, among 108 presumably normal soldiers examined consecutively for evidence of costoclavicular compression, the reaction to the attention position test was positive in only 3. Two of these had symptoms of costoclavicular compression, and 1 had no symptoms. The attention position test, as evidence of costoclavicular compression has, therefore, an accuracy slightly better than 99 per cent.

#### REPORT OF CASES

CASE 1.—H. W., a white man aged 28, was first seen in May 1945. His chief complaint was pain in the right scapular region of five years' duration.

*History of Present Illness.*—Five years previous to his admission he suffered frequent attacks of severe pain in the right scapular region while driving a truck. In the two years preceding his induction into the army he worked in the fire department and was entirely symptom free. He entered the armed forces on Dec. 14, 1944. Shortly after beginning his training he felt pain in the right scapular region radiating down the arm while carrying a pack or rifle. The arm would frequently become numb.

*Physical Examination.*—This revealed the fact that the pulse to the right arm was completely obliterated when the shoulders were thrown back in the attention position. There was no such change in the blood pressure in the opposite arm. The Adson maneuver elicited a negative reaction on both sides. The following tabulation indicates the blood pressure changes with the different tests.

	Normal	Adson Maneuver	Attention Position
Right arm.....	128/84	124/84	0/0
Left arm.....	124/84	124/84	124/84

When the Adson maneuver was first performed on the right, the patient simultaneously pushed the shoulder down and back and so produced a complete obliteration of the pulse and gave a false positive reaction. However, when the test was repeated with care being taken to have the patient keep his shoulder forward, the pulse was no longer shut off.

*Comment.*—This is a sample of a patient with the costoclavicular syndrome with no evidence of scalenus fibrosis. A false positive reaction to the Adson test was produced when the shoulder was not kept forward. This is the type of case in which scalenotomy could be erroneously performed, and it probably has been done in similar cases in the past.

**CASE 2.**—A youth aged 19 was first seen on July 19, 1945. He had entered active duty on May 29. The following is an abstract of his clinical record. His chief complaint was numbness of the right arm of five days' duration.

*History of Present Illness.*—One year previously he was engaged in farm work in which he would milk three to four cows by hand. After milking, he would carry two 3 gallon (11 liter) pails a distance of 110 feet (36 meters). He noticed that he would wake in the mornings with numbness in both hands. Normal sensation would return in the hands after shaking them a few minutes. He entered active duty on May 29, 1945, and on July 14 he went on a 7 mile (11,263 meter) hike with full pack. As soon as he got his pack and rifle on, the right hand and arm became numb. Previous to this time, carrying a rifle would produce temporary numbness. This particular attack, however, persisted until the time of examination five days later, although the numbness was then rapidly disappearing.

*Physical Examination.*—This showed that the right shoulder was considerably lower than the left. Blood pressure studies on both arms in various positions showed that the pulse beat on the right side was completely obliterated in the "attention position." The Adson maneuver produced a reduction in pulse beat on both sides. The following tabulation indicates the blood pressure readings.

	Normal	Adson Maneuver	Attention Position
Right arm.....	120/80	84/60	0/0
Left arm.....	120/80	90/80	100/90

*Comment.*—This patient suffered from costoclavicular compression on both sides, more so on the right. Symptoms were brought on at first by milking cows and carrying heavy pails and later by carrying a pack or rifle. The results of the Adson maneuver indicated that there was some fibrosis in both scalene muscles.

#### COMMENT

Among the 14 cases of costoclavicular compression studied, the Adson maneuver gave a specifically positive reaction in only 5. This indicates that in these 5 cases there was fibrosis of the scalenus anticus, probably a result of intermittent pinching of this structure between the clavicle and the first rib. The subjects were mostly all young men in whom symptoms had been present a relatively short time. It is probable that in an older age group with narrowing of the costoclavicular space a much higher incidence of fibrosis of the scalenus muscles would be present.

Compression of the subclavian artery and brachial plexus nerve trunks may occur at one of three places: (1) behind the scalenus anticus muscle; (2) between the clavicle and the first rib, and (3) beneath the pectoralis minor muscle.<sup>4d</sup> These three conditions are diagnosed by three separate maneuvers: (1) the Adson maneuver, (2) the shoulder attention position and (3) hyperabduction of the arm.

Patients with costoclavicular compression have probably been benefited by scaleniotomy in the past because the costoclavicular space is increased, which makes more room for the neurovascular structures. This increase in roominess is accomplished in two ways: (1) the first rib descends

when the muscle is cut, and (2) the muscle retracts, leaving one less bulky structure in the costoclavicular space.

The cases herein reported were all studied in military service. However, since resuming private practice, we have encountered 7 cases of costoclavicular compression. This leads one to believe that the condition is much more common than supposed and that it will be diagnosed more frequently as it becomes better known.

#### SUMMARY AND CONCLUSIONS

1. Evidence is presented to show that many symptoms attributed to the scalenus anticus muscle are actually due to costoclavicular compression. The neurovascular structures passing to the arm are intermittently compressed as in a vise the jaws of which consist of the clavicle and the cervical or first thoracic rib. This compression is readily produced by a simple test in which the pulse to the arm is markedly reduced or shut off when the shoulders are placed in the "attention position."

2. Many patients when being tested for scalenus anticus syndrome by means of the Adson maneuver will automatically push the shoulder down and back, producing occlusion of the pulse due to costoclavicular compression. This leads the examiner to believe that he is dealing with a scalenus anticus syndrome. Section of the scalenus anticus muscle may at times produce some benefit because of an increase in size of the costoclavicular space. However, the erroneous etiologic conception may account for some of the disappointing results reported.

3. Twenty-one patients complaining of vascular or neurologic disturbances of the arm were studied. Fourteen of these were found to be suffering from a costoclavicular compression syndrome. In all the pulse was reduced in volume or completely occluded when the shoulders were placed in the "attention position," an accuracy of 100 per cent on the affected side.

4. One hundred and eight presumably normal controls were studied. Only 4 had positive reactions to tests, and of these, 3 were found on further study to be suffering from the costoclavicular syndrome. Only 1 patient who was symptom free gave a positive reaction, which indicates that the test is over 99 per cent accurate.

5. Some patients were benefited by exercises aimed at strengthening the levator scapulae and trapezius muscles, although the follow-up was not adequate. If exercises fail, scaleniotomy and removal of the cervical rib or a portion of the first thoracic rib is recommended. Excision of the middle third of the clavicle is suggested as another possible method of therapy in intractable cases but it has not been tried.



## EXPERIMENTAL STUDIES IN VASCULAR REPAIR

### II. Strength of Arteries Repaired by End to End Suture, with Some Notes on Growth of Anastomosis in Young Animals

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CONSIDERABLE knowledge has been accumulated concerning the healing of arteries repaired by suture, the technical features of the operative procedure which favor a successful result and the influence of certain local pathologic processes on the outcome. Little or nothing is known about the strength of the sutured artery or the increase in circumference of the line of anastomosis during the period of body growth. The experiments herein recorded were carried out in an effort to answer the following questions: Does the artery repaired by end to end anastomosis have great or little resistance to disruption when tension is made on the suture line by direct pull? Does the repaired artery have great or little resistance to bursting from intraluminal pressure? Is there a curve of arterial healing similar to those established for the healing of other tissues? Does the line of suture in the anastomosed artery increase in size with increase in size of the artery itself in the growing animal? It was believed that an answer to these questions might make possible more intelligent management of patients for whom vascular repair was necessary.

#### STRENGTH OF THE ARTERY AS MEASURED BY BURSTING EXPERIMENTS

The experiments were carried out on adult dogs. With the use of sodium pentobarbital and with aseptic precautions, the common carotid arteries were exposed, divided and sutured end to end according to methods previously described.<sup>1</sup>

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1. Shumacker, H. B. Jr., and Lowenberg, R. I.: Experimental Studies in Vascular Repair: I. Comparison of Reliability of Various Methods of End-to-End Arterial Suture, to be published.

No anticoagulants were used. The dogs varied considerably in size, breed and age. They were all fed the ordinary laboratory diet. Specimens were removed at varying intervals after operation. They were stripped of the very loose external adventitia, moistened with saline solution and immediately subjected to increasing intraluminal pressures until bursting of the line of anastomosis or of the unsutured portion of the artery occurred.

After preliminary studies with mercury manometers, which were found inadequate because of the very high pressures required, and with various methods of producing pressure for the injection, the apparatus depicted in figure 1 was devised. A carbon dioxide tank was connected through a needle valve with a copper tube introduced into the upper portion of the side of a discarded small oxygen tank.

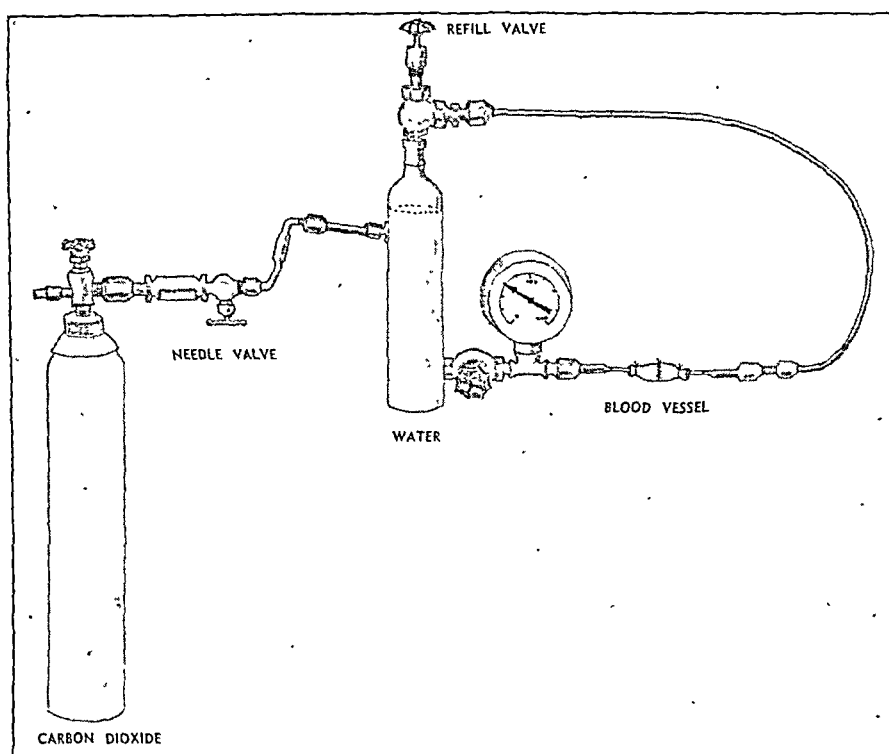


Fig. 1.—Apparatus used in the experiments to determine bursting points.

Another tube emerging from the lower portion of this tank was connected with a pressure gage recording up to 200 pounds and with a small metal cannula. A second cannula was fitted to the end of another tube connected with the top of the tank. The latter tube was used for filling the tank with water. This could be accomplished by opening the top valve on the upper side arm and aspirating water through the tube into the tank. The tank was kept nearly full with water at all times. Except when opened for refilling of the tank, the top valve was kept closed. The freshly removed specimen was secured into the circuit by fixing the two cannulas into the ends of the artery and ligating the vessel about the cannulas with heavy braided silk.

With the needle valve closed, the main valve on the carbon dioxide tank was then opened. The needle valve was turned just sufficiently to permit a slow, steady

increase in pressure. It was not possible to regulate precisely the rate of increase in pressure. However, the procedure was always carried out by the same person, and an effort was made to have a comparable rate of increase of pressure in all experiments; it is believed that little variation occurred. Close watch was kept on the gage and the adjacent vessel. If a leak in the suture line or through the artery wall occurred before bursting, the pressure at which this took place was recorded. The increasing pressure was continued until either the line of anastomosis or the vessel wall broke; the pressure at which this event took place was similarly recorded. The point of bursting was taken as that at which the leak was sufficiently great to cause cessation in rise of pressure as recorded on the gage, or a tendency for the pressure to fall. It will be noted that the water entered the artery at one end and that the pressure continued to rise as the pressure in the tank was increased and as the fluid and air in the long refilling arm became compressed, until equilibrium was reached. In a sense, this arrangement simulated the driving force of the heart and the resistance of the distal vascular bed.

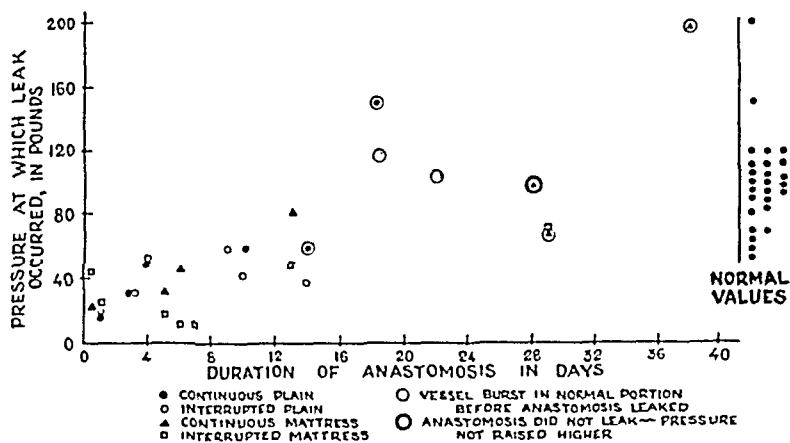


Fig. 2.—Strength of arteries repaired by end to end suture, as indicated by the intraluminal pressure at which a leak at the suture line first occurred. In this chart, as well as in figure 3, the values for the specimen studied thirty-eight days after repair may not be entirely accurate, since some technical difficulty with the apparatus was encountered at that time.

In figure 2, the pressures are recorded at which the anastomosis first began to leak and are compared with values for the normal carotid artery. Twenty-eight observations were made on leaking of the suture line. Twenty-six observations are recorded of the point at which the normal vessel first leaked or at which it burst in those instances in which the initial leak was simultaneous with bursting of the vessel wall. Several facts are evident. In the first place, there was a fairly wide variation. In spite of the variable results, however, it will be seen that the general trend toward increase in resistance to leaking along with an increase in the age of the anastomosis corresponds roughly to the type of curve which has been found representative of the gain in

strength of other sutured tissues. It is evident that the repaired artery withstands, without leaking, pressures far in excess of arterial pressures encountered even in hypertension. In eight hours the pressures at which a leak first occurred were 22 and 46 pounds, or 1,113 and 2,326 mm. of mercury. The lowest pressure at which any of the anastomoses was found to leak was 12 pounds, or more than 600 mm. of mercury. It is seen that the pressures at which a leak occurred increased rapidly with the duration of the anastomosis. Only 2 of the 14 specimens examined within seven days first developed a leak at pressures as high as the lowest normal values, whereas all but 2 of the 14 specimens tested after nine days or longer leaked at pressures at or above the lowest normal values. Furthermore, it will be noted that of the 9 arteries tested fourteen days or more after repair, all save 3 failed to leak at all at pressures at which the normal portion of the vessel wall leaked or burst; 1 of the 3 arteries did not leak at 100 pounds, which was the maximal pressure to which it was subjected. These observations tend to indicate that the sutured artery rapidly regains relatively normal resistance to high intraluminal pressures and that after fourteen days or longer it tends to be more resistant to leaking than is the normal artery.

In figure 3, pressures are recorded at which the line of anastomosis and the normal artery burst. It will be seen that the curve is similar to that recorded in figure 2. There was greater variation in values obtained within the first week after repair. In a comparison of the two charts, it will be seen that there was often a significant difference in the pressures at which any given anastomosis first leaked and then finally burst, whereas the normal artery wall tended to burst at pressures only slightly higher than those at which a leak first occurred, or burst simultaneously with the first leak. Eight hours after repairs the pressures at which the suture line burst were 40 and 60 pounds, or somewhat over 2,000 and 3,000 mm. of mercury, respectively. Twenty-four hours after repair the values ranged from 22 to 95 pounds. As early as five days after repair one suture line failed to burst at a pressure sufficient to burst the unsutured portion of the artery. After two weeks all but 3 of the 9 vessels tested did not burst at pressures sufficient to burst the normal portion of the artery, and 1 of the 3 vessels did not leak at the highest pressure (100 pounds) to which it was subjected. In both figures 2 and 3, values with different methods of repair are indicated. In view of the rather wide variation in results and the small numbers in each group, it is felt that no conclusion can be reached concerning the relative resistance of various types of anastomosis to high intraluminal pressure.

It is apparent that in studies such as these it would be desirable to correlate the thickness of the wall of each individual artery with the pressure at which a leak or burst occurred. Since the pressure is evenly distributed to all portions of the wall of a tubular structure, the resistance to rupture is dependent chiefly on the thickness of the wall and the innate characteristics of the tube. It is, unfortunately, not possible to measure accurately the thickness of the wall of an artery. It varies with spasm or dilatation of the vessel. If the vessel is compressed between two glass slides and the space between is measured to yield twice the thickness of the artery wall, the results differ according to the pressure made on the vessel. If in each case the sutured portion of the artery and a normal intact segment had been tested separately, one could have expressed the result in percentage of normal. This was

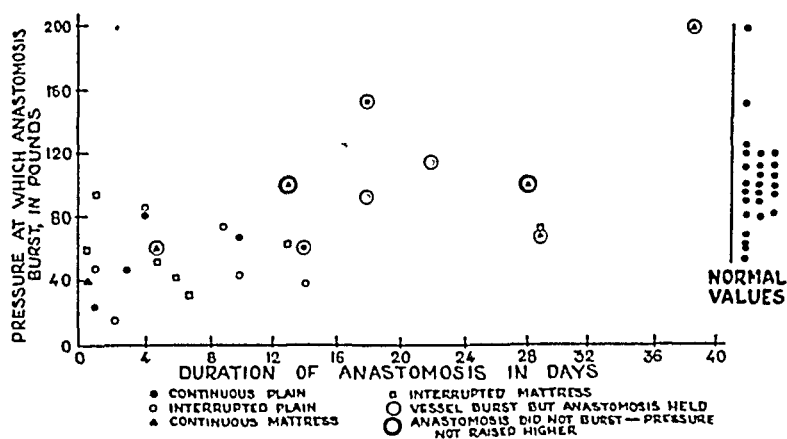


Fig. 3.—Strength of arteries repaired by end to end suture, as indicated by the intraluminal pressure at which the suture line burst.

not done. In each instance, however, we made careful observations to see whether the line of the anastomosis or the normal portion of the artery first give way; as we have pointed out, many of the suture lines failed to leak or burst at pressures which ruptured the artery itself.

It is not surprising that there was considerable variation in the results. The dogs varied in size and age and the size of the carotid arteries differed considerably. Furthermore, it is almost certain that we were never able to strip precisely the same amount of adventitia from all the vessels. That the adventitia lends strength to the vessel is evident. One portion of a control artery with its adventitia intact was found to burst at 62 pounds, for example, while an adjacent portion of the same vessel carefully stripped of the gross external adventitia burst at a pressure of only 24 pounds.

## BREAKING FORCE NECESSARY TO PULL APART THE SUTURED ARTERY

Adult dogs were operated on as described in the previous section. All the end to end sutures were carried out with the continuous mattress technic. At varying intervals after operation the specimens were excised. The diameter of the artery was measured, and the loose adventitia was removed. Sufficient length of the artery was excised to permit testing of both the segment containing the suture line and an adjacent normal segment. A number of normal carotid arteries of dogs were similarly prepared for study. The specimen was then measured as carefully as possible. In order to calculate the cross sectional area of the sutured artery, the vessel was gently compressed between two glass slides of known thickness. The thickness of the two slides and the interposed compressed artery was measured with a micrometer accurate to 0.001 inch (2.5 mm.). Simultaneously, the width of the compressed vessel was measured with a ruler of similar accuracy. The artery being compressed between the slides, its cross sectional area was converted for all practical purposes into a rectangle. Presumably, any diminution in thickness by too much compression would result in a corresponding increase in width. By subtracting the thickness of the two slides from the first measurement and multiplying the remainder by the second measurement, the surface area of a cross section of the vessel was obtained. These measurements were made by one observer.

As soon as the measurements were completed, the artery was again moistened with solution of sodium chloride and was divided into two segments, each of which was tested on a Henry L. Scott apparatus designed for determining the tensile strength of suture materials. Each end of the specimen was fixed in the metal jaws of the machine after the ends of the vessel had been carefully wrapped in gauze so as to prevent tearing of this portion of the vessel wall from the pinching force of the clamps. One of the clamps was attached to a gage which recorded force in pounds of pull and could be read in increments of  $\frac{1}{8}$  pound. An automatic device fixed the indicator at the point at which breaking occurred. The other clamp was attached to a cable on which a pull was exerted by the turning of a large wheel. The increase in pull exerted was at a nearly uniform rate. The sterilized 000000 Deknatel suture used in the vascular suture broke in single strands at a force averaging  $\frac{1}{4}$  pound.

The force necessary to break normal carotid arteries varied from 3.87 to 10 pounds. The force necessary to break the anastomoses varied rather widely (table). It was our hope that consideration of the surface area would yield more information concerning the rate in gain of strength of the sutured artery. However, the same wide variation in the force necessary to pull apart sutured arteries and normal arteries was found. The figures for the normal arteries ranged from 658 to 1,810 pounds per square inch, with an average of 1,224 pounds. When two carotid arteries from the same animal were tested, there was often close correlation of the two in the breaking force and in the "tensile strength" in pounds per square inch; in some, however, the figures for the two arteries were very different. The tensile strength of one, indeed, was nearly twice that of the contralateral artery.

When the breaking force of the suture line was compared with that of an adjacent segment of the same artery and the result expressed in the percentage of normal, a curve was obtained which appears to denote the real trend of the gain in strength of the sutured vessel. In figure 4, these data are plotted in comparison with similar data recently obtained by Fast, Nielsen and Dennis<sup>2</sup> for healing of abdominal wounds. These authors studied the force necessary to pull apart the abdominal wall of rabbits after having made and repaired a rectus incision. The silk sutures were left intact, and the abdominal wall as a whole was tested except for the skin, which was removed. By performing identical studies of the normal abdominal wall on the other side of the midline, they were able to express the results in percentage of normal. It will be seen that our data follow the mean curve of Fast,

*Force Necessary to Pull Apart Anastomoses*

	Duration of Anastomosis, in Days	Breaking Force, in Pounds	"Tensile Strength," in Pounds per Square Inch
Sutured arteries.....	3	2.125	352
		3.125	727
	6	3.375	485
		1.875	582
	10	3.75	765
	14	5.375	1,340
	20	5.375	1,220
		6.5	1,470
	22	3.875	626
	28	4.0	638
Normal arteries..... (32 specimens)	34	3.5	555
	40	6.375	776
	Range	3.875-10	658-1,810
	Average	6.8	1,224

Nielsen and Dennis surprisingly closely, only the value for the thirty-four day specimen falling far from their curve.

It is not surprising that the absolute values for our normal and sutured arteries varied widely. As applied to metallurgy, tensile strength is the quotient of the force employed and the cross sectional area of the object within the elastic limit of that particular material. In our studies, the determinations have been carried to the breaking point and hence might better be termed studies of disruptive strength than studies of tensile strength. Since, however, a small increment of force reflects an appreciably larger strain on the material once the elastic limit has been reached, only a small difference in force exists between tensile and disruptive strength. Unfortunately, measurement of the cross sectional area of the artery by the method we employed is undoubtedly subject to considerable error, though the method is osten-

2. Fast, J.; Nielsen, C., and Dennis, C.: Rate of Gain in Strength in Sutured Abdominal Wall Wounds, Surg., Gynec. & Obst. **84**:685-688, 1947.

sibly sound. In addition, there are certain variables which cannot be controlled. Precisely the same amount of adventitia cannot be removed from each specimen, and, as we have pointed out before, the adventitial layer imparts a great deal of strength to the vessel. There are undoubtedly variations in the strength of arteries from one animal to another, and from one artery to another in the same animal. In such an experiment as we have performed it is impractical to use litter mates for study, though this might have been advantageous. It appears, however, that comparison of the sutured and normal segments of the same artery and calculation of results in percentages of normal is a sound method for evaluating the strength of the anastomosis.

#### INCREASE IN SIZE OF ANASTOMOSIS IN GROWING ANIMALS

Both common carotid arteries of 4 small puppies were divided and anastomosed with continuous mattress sutures. As the animals and

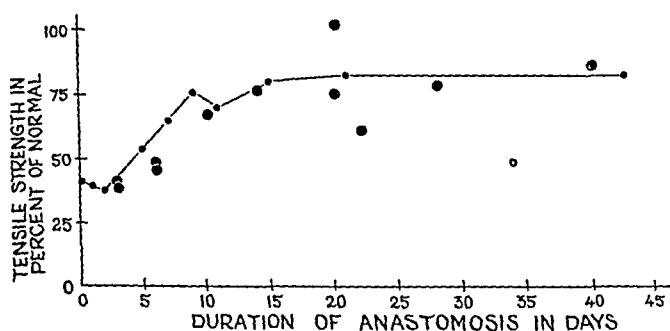


Fig. 4.—Strength of arteries repaired by end to end suture, as measured by the force necessary to pull apart the line of anastomosis. The data are expressed in percentage of normal, the normal values in each instance being determined by pulling apart an adjacent normal portion of the repaired artery. The experimental data are recorded as large solid circles and are compared with the mean curve obtained by Fast, Nielsen and Dennis for gain in strength of the sutured abdominal wall.

their carotid arteries grew in size, the line of suture appeared to increase in size correspondingly. The vessels of 2 dogs were examined approximately one month after suture, and the diameter of the 4 sutured vessels was the same at the line of suture as that of the unsutured portion of the artery. The vessels of 2 dogs were examined six months later. The dogs had gained in weight from 2.9 to 9.8 Kg. and from 5.1 to 14.5 Kg., respectively. The diameters of the carotid arteries had increased between 30 and 45 per cent. The line of anastomosis appeared to be quite as large as the remainder of the vessel. Since these preliminary studies seemed to indicate that the sutured portion of an artery grows with the growth of the vessel itself, no further experiments were conducted.



## COMMENT

The studies presented demonstrate that the artery recently repaired by end to end suture breaks with relative ease when tension is placed on the line of suture by direct pull but withstands exceedingly high intraluminal pressure without leaking or bursting. If our relatively small number of observations can be interpreted as demonstrating the gross trend of healing, we may infer that the repaired artery has only about one-third the normal strength to resist disruption by direct pull during the first few days but has about three-quarters the normal strength by the end of the second week. Our studies demonstrate that the repaired artery, on the other hand, will withstand, without leaking, pressures many times as high as systolic blood pressure even within a few hours after repair, and that it is likely to be more resistant to leaking with high pressures than the unsutured portion of the artery after two weeks have passed. These experiments indicate clearly that one need have little fear of disruption of the sutured artery from the force of the blood pressure. If the anastomosis is left dry and has been accomplished without tension, there is little or no hazard of subsequent disruption and hemorrhage. If the ends of the artery can be approximated only by relaxation of tension by proper posturing of the part, as is sometimes necessary in the surgery of aneurysms and fistulas of the axillary, brachial, popliteal and other peripheral vessels, one must maintain the extremity in the optimal position for some time. We do not feel that our studies yield conclusive evidence concerning the necessary length of time for avoidance of tension on the suture line after repair, but they suggest that at least a two week period, and perhaps a longer time, is essential. In certain vascular operations vessels which appear capable of being brought together only under tension can be successfully approximated, as is not infrequently the case in the subclavian-pulmonary artery operation of Blalock.<sup>3</sup> In none of these cases has disruption occurred. It is entirely likely that when vessels can be brought together with 00000 or 000000 silk sutures one can assume that they are held without undue tension.

The ultimate functional success of vascular anastomoses in the young depends on the growth in size of the suture line as the artery increases in circumference. Otherwise, the result would be compromised by development of a functional stricture. Our preliminary observations suggest that the circumference of the line of anastomosis and that of the unsutured wall of the artery increase comparably.

Our studies throw some light on the rate of healing of the sutured artery and indicate that the trend of gain in strength is comparable to

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3. Blalock, A.: Physiology and Surgical Treatment of Congenital Cardio-Vascular Defects, *Bull. New York Acad. Med.* **22**:57-80, 1946.

that observed in other tissues by Harvey and his associates and by others.<sup>4</sup> We should like to emphasize, however, that our studies are not presented as representing statistically accurate curves of gain in strength. In most such experiments absorbable suture material has been used so that the tests could be performed on tissues free of sutures; in our studies the tests were performed on anastomoses with the original silk sutures intact. We have pointed out the role of the adventitia in the strength of the sutured artery and the improbability that the adventitia can be stripped to a precisely comparable degree in each specimen. We have also discussed certain other possible variables, such as weight, size, age and breed of the animal. In addition, though we have carried out sufficient studies to indicate the trend, we have not performed the numerous experiments which would be necessary to establish a statistically significant mean curve of increase in strength. It is of interest that the trend demonstrated is quite similar to the curves established for the healing of other tissues. The data obtained with our determinations of the breaking force followed remarkably closely the curve for gain in strength of the abdominal wall with intact silk sutures presented by Fast, Nielsen and Dennis. Our studies would indicate that any future experiments designed to establish more precisely the rate of increase in strength of the sutured vessel may best be expressed in percentage of normal of the vessel which itself was used for the repair.

#### CONCLUSIONS

1. The artery anastomosed by end to end repair appears to gain in strength in a fashion similar to that of other sutured tissues.

2. The force necessary to break the recently sutured artery by direct pull is not great, but the sutured artery withstands, without leaking, intraluminal pressures far in excess of systolic blood pressure.

3. Preliminary studies indicate that the circumference of the artery at the line of anastomosis increases in the growing animal comparably to the increase in circumference of the unsutured portion of the artery.

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## RETROCAVAL URETER

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THE VASCULAR anomaly which results in a venous trunk lying anterior to the ureter so that the latter structure must completely encircle it en route to the bladder has been variously described as a post-caval ureter, a precaval ureter and a circumcaval ureter. We are unable to offer a more accurately descriptive term, but it must be realized that although these terms would suggest a ureteral anomaly it is actually a vascular abnormality. That this vascular variation is premiant is attested by the fact that the case reported herein is the thirty-seventh recorded instance, and only twice previously has the diagnosis been made preoperatively. This condition, by virtue of its infrequency and the associated potential seriousness of the resultant lesion along with the complexity of its surgical correction, demands more frequent preoperative diagnosis. The treatment will be discussed in the light of the present exiguous literature and the reported cases analytically tabulated.

The embryologic considerations have been discussed in varying detail in numerous reports and will be omitted in this paper. Suffice it to say that this rarest of congenital anomalies is due to vascular variation by the persistence of one of the embryonic veins during the formation of the vena cava and that the obstructive uropathy is an incidental occurrence. Ureteral obstruction with hydroureter or pyelocystitis or both was recorded in 24 of the 36 cases previously reported. In 1 case the status of the urinary tract was not reported. The cause of the obstruction in our opinion is dependent more on the ureter being wedged in the crotch formed by the vena cava and the vertebral vein than on pressure between the vena cava and the posterior abdominal wall or between the vena cava and the aorta.

### SYMPTOMATOLOGY

The subjective findings vary from those of ureteral colic to those of intractable pyelonephritis and hematuria. Some of the patients are asymptomatic and the condition is first observed as an incidental finding at necropsy.

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## DIAGNOSIS

A preoperative diagnosis has been made on only two previous occasions (Harrill; Greene and Kearns). In Harrill's patient the symptoms of ureteral obstruction were evident, and the diagnosis was made by means of stereoscopic pyelograms. In the case reported by Greene and Kearns a calculus had been passed previously, and shortly before the diagnosis of circumcaval ureter was made the patient experienced severe ureteral colic associated with hematuria. The diagnosis was established since the pyelograms revealed distention of the upper part of the ureter, which ended abruptly when the ureter passed over the body of the third lumbar vertebra in a superior and medial direction. In our case the diagnosis was made on essentially the same criteria as those described by Greene and Kearns.

The most suggestive diagnostic criteria for circumcaval ureter are as follows.

A. In the lateral roentgenograms the ureter, instead of maintaining a position distinctly anterior to the vertebral column in the region of the third or fourth lumbar vertebral bodies, lies in close apposition (Randall and Campbell).

B. The stereoscopic pyeloureterograms demonstrate the ureteral curvature to be such as "to include a structure having the diameter and position of the vena cava" (Harrill).

C. The ureter is displaced toward and generally overlies the mid-line, usually in the region of the third and fourth lumbar vertebra.

D. The ureter presents in its upper portion a falciform curve, and if there is present obstruction the ureterectasis ends abruptly at the medial portion of the curve as it courses downward and overlies the third and fourth lumbar vertebrae.

E. The abnormality is a lesion on the right side and has been known to occur bilaterally only once and that in an acardiac monster with a bilateral vena cava (Gladstone).

## TREATMENT

In 6 of the 36 patients reported on a primary nephrectomy was employed. These patients constitute part of the group of 15 surgically treated patients (Randall and Campbell; Derbes and LaNasa; Shih; Gruenwald and Surks; Wilson and Herzlich). In one instance a secondary nephrectomy was necessary since after the plastic repair of the ureteral abnormality calculi and infection intervened (Nourse and Moody).

In the case reported by Young a calculus was removed from the upper part of the ureter and no further surgical procedure undertaken

since it was felt that the anomaly was of no obstructive significance. The author's postoperative observations were reported to have substantiated this decision.

Various types of plastic procedures on the ureter were done in 7 instances (Kimbrough; Uebelhör; May; Harrill; Greene and Kearns; Lowsley; Nourse and Moody). The plastic operation most commonly employed was section and reanastomosis of the ureter after its removal from around the vena cava. To Kimbrough goes the distinction of first observing a postcaval ureter at operation and successfully performing ureteral section and reanastomosis. Harrill was the first to diagnose this condition preoperatively. He divided the renal pelvis, and after the ureter was freed from its caval position the pelvis was reanastomosed. Lowsley, on the other hand, divided the ureter at its vesical extremity and after removing it from the vena cava reimplanted it into the bladder. Because of a ureteral stricture in its immediate superovesical portion a second operation was necessary. This was followed by the development of an abscess which devitalized the ureter, and a cutaneous ureterostomy was the final solution.

It seems to us that in instances in which the renal destruction has not progressed to an irreparable stage a plastic operation or a combination of such procedures is the therapeutic solution. Furthermore, the actual excision of the ureteral stricture would seem to offer permanent success.

In the following table the various cases recorded are tabulated. It will be noted that there are 27 males in this series. As several authors have pointed out, the preponderance of males is probably due to the fact that most of the persons were seen as cadavers and in this group males predominate. In the operative cases it will be seen that again the males predominate; however, the series is too small to be of statistical significance. In 24 instances of retrocaval ureter there was an associated obstructive uropathy.

There have been reported a total of 36 persons with retrocaval ureter during the past fifty-four years. All patients were seen on the dissecting table until 1935, when Kimbrough observed the first patient at operation. Harrill, in 1940, was the first to diagnose this abnormality preoperatively.

#### REPORT OF A CASE

A farmer of 44 years consulted us on the advice of his family physician because of a recent attack of ureteral colic on the right side associated with hematuria. His subjective symptoms were relieved after two injections of morphine.

On physical examination nothing of note was discernible. The urinalysis showed moderate pyuria with microscopic hematuria. Studies of the blood

*Chronologic Tabulation of Cases Reported*

Author	Year	Sex	Age	Obstructive Uropathy	Time of Diagnosis	Comment
Hochstetter	1893	M	Weeks	No	Necropsy	Acardiac fetus
Gladstone	1905	M	Term	No	Necropsy	
Kolisko	1909	M	55 yr.	Yes	Necropsy	Renal agenesis, left
Gladstone	1909	M	84 yr.	Yes	Necropsy	
Jacobson	1927	M	72 yr.	Yes	Necropsy	
Jacobson	1927	M	1 yr.	No	Necropsy	
Wicke	1927	M	58 yr.	No	Necropsy	
Kengyel	1928	F	57 yr.	Yes	Necropsy	First patient seen clinically; lesion diagnosed at second operation and successfully repaired by section and reanastomosis
Gierke	1928	M	16 yr.	Yes	Necropsy	
Skamnakis	1931	M	50 yr.	Yes	Necropsy	
Kimbrough	1935	M	20 yr.	Yes	Operation	
Rotter	1935	M	49 yr.	Yes	Operation	Double postrenal vena cava, right
Rotter	1935	..	.....	No	Necropsy	Bilateral postrenal vena cava
Randall and Campbell	1935	F	25 yr.	Yes	Operation	Nephrectomy
Randall and Campbell	1935	F	55 yr.	Yes	Operation	Nephrectomy
Derbes and Dial	1936	?	Adult	Yes	Necropsy	Ureteral section and reanastomosis; nephrostomy and nephropexy; recovery
Derbes and Dial	1936	?	Adult	Yes	Necropsy	
Uebelhör	1936	F	36 yr.	Yes	Operation	
Derbes and LaNasa	1937	F	42 yr.	Yes	Operation	Nephrectomy
Wren	1937	M	Adult	No	Necropsy	Nephrectomy
Shih	1937	M	44 yr.	Yes	Operation	
Adachi	1937	M	42 yr.	?	Necropsy	Bilateral postrenal vena cava
Adachi	1937	F	40 yr.	No	Necropsy	Bilateral postrenal vena cava
May	1938	M	17 yr.	Yes	Operation	Ureteral section and reanastomosis; pyelotomy; nephrostomy; nephropexy
Palazzi, Rached, Sanchez and Rincon	1939	M	Adult	No	Necropsy	First instance of preoperative diagnosis; ureter passed around double vena cava; section above the ureteropelvic junction with reanastomosis
Antopol and Yelin	1939	F	72 yr.	Yes	Necropsy	
Pick and Anson	1940	M	44 yr.	No	Necropsy	
Harbach	1940	M	20 yr.	Yes	Operation	
Harrill	1940	M	46 yr.	Yes	Preoperative	
DeCarlo	1941	M	60 yr.	No	Necropsy	Nephrectomy
Gruenwald and Surks	1943	M	Adult	No	Necropsy	
Wilson and Herzlich	1944	M	21 yr.	Yes	Operation	Nephrectomy
Nourse and Moody	1946	M	21 yr.	Yes	Operation	Unsuccessful ureteral anastomosis due to calculus; nephrectomy
Greene and Kearns	1946	M	29 yr.	Yes	Preoperative	Ureteral section and reanastomosis
Lowsley	1946	M	44 yr.	Yes	Operation	Ureteral section at the bladder with reimplantation, nephrostomy; subsequent abscess at the site of vesical implantation requiring cutaneous ureterostomy (left kidney nonfunctional)
Young	1947	F	24 yr.	Yes	Operation	Cause of obstructive uropathy thought to be ureteral calculus rather than the post-caval ureter and for this reason the calculus was removed and no plastic procedure done to change the course of the ureter; disappearance of ureteral dilatation observed 8 months postoperatively

revealed no anemia and a normal cytologic picture. Chemical examination of the blood and immunologic studies revealed nothing abnormal.

The cystoscopic examination revealed a slightly edematous right ureteral orifice but no other signs of vesical abnormality. On the introduction of ureteral catheters into both renal pelves the left kidney was found to be normal functionally and morphologically. The right kidney was virtually functionless as studied on the basis of excretion of dye. The ureteropyelogram demonstrated a markedly hydronephrotic pelvis and calyces with the upper region of the ureter dilated. This region prescribed a typical falciform curve, with the terminal portion of the



Fig. 1.—Ureteropyelogram showing falciform curve in ureter which in its lower portion overlies the body of the third lumbar vertebral body.

dilated ureter overlying the third lumbar vertebral body and at this point crossing the midline of the body. It was on the basis of this last criterion that the diagnosis of retrocaval ureter was made which was confirmed at operation.

At operation the right kidney was found to be greatly enlarged. The pelvis was huge, and the upper portion of the ureter took a normal downward course and then suddenly turned and passed under the vena cava. When a portion of the vena cava was isolated below the point where the ureter passed under this structure, the ureter was again visualized as it emerged from behind the vessel, and after encircling the vessel it proceeded in a normal course toward the bladder. At the pelvic brim the ureter had assumed its normal relationship with the iliac

vessels. The ureter was severed near the bladder after ligation and dissected free. It was found difficult to extract the ureter from under the vena cava, and for this purpose it was necessary to mobilize the vena cava partially. The hydronephrotic portion of the ureter suddenly ceased at the point behind the vena cava where the ureter was wedged in a crotch formed by a vertebral vein and the vena cava. It would seem that this relationship was the cause of the hydronephrosis rather than the abnormal association of the ureter and the vena cava. After the ureter was entirely free and removed from behind the vena cava the renal pedicle was ligated and the kidney and ureter removed.

The patient's postoperative course was uneventful, and he has enjoyed an active, healthy existence during the past eighteen months.



Fig. 2.—Operative specimen showing pyelectasis and the course of the ureter in its circumvascular path around the vena cava, which is represented by the test tube.

#### SUMMARY

An additional case of retrocaval ureter is added to the existing literature, which brings the total number of reported cases to 37. The patient was subjected to nephrectomy and ureterectomy because of an inadequately functioning kidney.

The literature is reviewed, and the previously reported cases have been tabulated. A complete bibliography is appended.



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## ACUTE MESENTERIC LYMPHADENITIS

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**A**CUTE mesenteric lymphadenitis is a symptom complex characterized by abdominal pain and tenderness. For the patient suspected of having this condition, the presence of acute appendicitis cannot be excluded either by the history, the physical examination or the laboratory findings. Because of this difficulty in differentiation, with rare exceptions operation is urgently indicated when either diagnosis is made.

During the five years between July 1, 1941, and Aug. 1, 1946, there were admitted to Duke Hospital 1,604 patients with the symptoms and signs of an acute condition in the abdomen which led to treatment by appendectomy. Of these, 931 had acute appendicitis. The remaining 673 patients had grossly normal appendixes; in this group, no cause for the abdominal pain was found in 185 patients, while 220 patients had one of a large number of diseases, the most common being hemorrhage from a ruptured graafian follicle, pelvic inflammatory disease and gastroenteritis. In 268 of the 673 patients with grossly normal appendixes, enlargement of mesenteric lymph nodes was encountered, and for these the diagnosis was nonspecific mesenteric lymphadenitis. Thus 1 patient in every 6 admitted because of an acute condition within the abdomen and treated by means of appendectomy had mesenteric lymphadenitis.

In spite of the frequent occurrence of acute mesenteric lymphadenitis, little definite information is available regarding the etiology, and considerable difference of opinion exists as to accuracy of differential diagnosis and proper treatment. Wilensky,<sup>1</sup> who has contributed several important summaries on the etiology as well as other aspects of mesenteric lymphadenitis, expressed the belief that it is a secondary

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1. Wilensky, A. O.: (a) General Abdominal Lymphadenopathy with Special Reference to Nonspecific Mesenteric Lymphadenitis, *Arch. Surg.* **42**:71-125 (Jan.) 1941; (b) Chronic Intra-Abdominal Lymphadenopathy with Special Reference to Chronic Nonspecific Mesenteric Adenitis, *Surgery* **9**:787-820 (May) 1941; (c) Acute and Chronic Intra-Abdominal Lymphadenopathy, *Surg., Gynec. & Obst.* **72**:1060-1069 (June) 1941.

manifestation of another process in the body, usually infectious. Ireland<sup>2</sup> has also summarized the suggested possible causes, which range from a foreign body to a virus. Many<sup>3</sup> believe that the appendix usually serves as the portal of entry for the offending agent. Wilensky<sup>1</sup> and Klein,<sup>4</sup> however, were of the opinion that only a congenital anomaly of the lymphatic drainage of the appendix may incriminate this structure as the site of the initial lesion.

Gage<sup>5</sup> has reported positive cultures of 93 per cent of 65 nodes removed, but others<sup>6</sup> have found the nodes usually sterile. Oxyuris vermicularis in the appendix was found by Ingegno<sup>7</sup> in 1 case, by Ireland<sup>2</sup> in 1, by Marshall<sup>6d</sup> in 6 and by Heusser<sup>6a</sup> in several cases. No cultures of a virus have been reported, although a virus has been suggested as the causative factor. Definite proof of a single etiologic agent is lacking.

Since the comprehensive papers by Wilensky in 1941 and the review by Postlethwait, Self and Batchelor<sup>8</sup> in 1942, several publications have appeared which are of interest particularly from the

2. Ireland, J.: Etiologic Factors of Mesenteric Lymphadenitis, *Arch. Surg.* **36**:292-302 (Feb.) 1938.

3. Lamson, O. F.: Mesenteric Lymphadenitis and Acute Appendicitis, *S. Clin. North America* **11**:1061-1063 (Oct.) 1931. Speese, J.: Mesenteric Adenitis, *Pennsylvania M. J.* **32**:225-228 (Jan.) 1929. Coleman, E. P.: Acute Mesenteric Lymphadenitis, *Tr. West. S. A.*, 1934, p. 129; *West. J. Surg.* **43**:193-198 (April) 1935. Short, A. R.: Symptoms Due to Mesenteric Lymphadenitis, *Lancet* **2**:909-912 (Nov. 3) 1928. Segar, L. H., and Rosenak, B. D.: Non-Tuberculous Mesenteric Lymphadenitis in Childhood, *Am. J. Digest. Dis.* **2**:356-360 (Aug.) 1935. Powers, J. H.: Unusual Inflammatory Lesions of Ileocecal Region, *Ann. Surg.* **103**:279-289 (Feb.) 1936. Porumbaru, I.: Lymphdrüsenentzündung der Ileo-Coecalgegend, *Zentralbl. f. Chir.* **65**:1913-1916 (Aug. 27) 1938. Luzuy, M.: Syndrome appendiculaire et adenite mesenterique aigue, *Rev. de chir., Paris* **77**:307-310 (April) 1939. Larghero I. P.: Adenitis supurados del mesenterio, *An. Fac. de med. de Montevideo* **23**:531-584, 1938. Brown, A. E.: Ileocecal Lymphadenitis in Children, *Surg., Gynec. & Obst.* **65**:798-806 (Dec.) 1937.

4. Klein, W.: Nonspecific Mesenteric Adenitis, *Arch. Surg.* **36**:571-585 (April) 1938.

5. Gage, I. M., in discussion on Wise, W. D.: Mesenteric Lymphadenitis, *Ann. Surg.* **109**:827-836 (May) 1939.

6. (a) Heusser, H.: Die Schwellung der mesenterialen Lymphdrüsen, *Beitr. z. klin. Chir.* **130**:85-98, 1924. (b) Von Sassen, W.: Bakterienbefunde bei Lymphadenitis ileocolica simplex, *Zentralbl. f. Chir.* **66**:1832-1835 (Aug. 12) 1939. (c) Goldberg, S. L., and Nathanson, I. T.: Acute Mesenteric Lymphadenitis, *Am. J. Surg.* **25**:35-40 (July) 1934. (d) Marshall, C. J.: Simple Ileo-Cecal Lymphadenitis, *Brit. M. J.* **1**:631-632 (April 14) 1928.

7. Ingegno, A. P.: Syndrome of Acute Mesenteric Lymphadenitis and Its Differentiation from Acute Appendicitis, *M. Rec.* **148**:298-301 (Oct. 19) 1938.

8. Postlethwait, R. W.; Self, W. O., and Batchelor, R. P.: Nonspecific Mesenteric Lymphadenitis, *Am. J. Surg.* **57**:304-315 (Aug.) 1942.

standpoint of differential diagnosis and indications for operation. Bothe and Pote<sup>9</sup> reviewed 154 cases and stated that abdominal exploration should be performed in all instances:

. . . first, lest an acute appendix which should be removed be overlooked; second, because laparotomy seems to be beneficial to the condition and may reveal any obstructive adhesions which should be corrected; third, because the type of after-treatment is influenced by the presence or absence of lymphadenitis; and fourth, because any possible portal of entry of infection should be removed.

Braithwaite<sup>10</sup> discussed the mechanism of production of gastric symptoms, particularly pylorospasm, by ileocecal disease, giving the etiologic factors as chronic appendicitis, nonspecific ileocecal adenitis and tuberculous ileocecal adenitis. He felt that ileocecal adenitis could be diagnosed from the presence of spasm of the lower portion of the ileum and the ileocecal valve, as demonstrated by roentgenologic studies. Fifteen cases of chronic ileocecal adenitis were reported. Tilley<sup>11</sup> reviewed his 69 cases and concluded that "operation with removal of the appendix is indicated when acute appendicitis cannot be ruled out; with a probable diagnosis of mesenteric lymphadenitis, treatment should be conservative."

King<sup>12</sup> reported on 84 patients and stated: "It is as yet impossible to diagnose the lesion definitely without laparotomy." Nevertheless, in 35 of his 84 cases no operation was performed. He reported on a patient hospitalized three days and then discharged with a diagnosis of mesenteric lymphadenitis. The patient returned one week later with a perforated appendix and abscess. Aird<sup>13</sup> observed 37 cases of mesenteric lymphadenitis in one year, but he stated that this figure was only an approximation as "a considerable number of children in whom a diagnosis of nonspecific adenitis has been made in the outpatient department have not been admitted but have been confidently allowed to go home." Coleman<sup>14</sup> stated, in a more recent review of his cases, that immediate appendectomy was routinely advised because "we have seen too many instances in which our preoperative diagnosis was

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9. Bothe, F. A., and Pote, H. H.: Mesenteric Adenitis Associated with Appendicitis, *Internat. Clin.* **4**:77-88 (Dec.) 1941.

10. Braithwaite, L. R.: Ileo-Gastric Syndrome, *Brit. J. Surg.* **30**:15-22 (July) 1942.

11. Tilley, J. H.: Acute Nonspecific Mesenteric Lymphadenitis, *Am. J. Surg.* **57**:472-476 (Sept.) 1942.

12. King, W. E.: Acute Nonspecific Mesenteric Adenitis, *Am. J. Surg.* **64**:92-94 (April) 1944.

13. Aird, I.: Acute Nonspecific Mesenteric Lymphadenitis, *Brit. M. J.* **2**:680-682 (Nov. 17) 1945.

14. Coleman, E. P.: Mesenteric Lymphadenitis, *Am. J. Surg.* **72**:879-882 (Dec.) 1946.

mesenteric lymphadenitis but upon opening the abdomen a distended, acutely inflamed appendix was found."

It is evident from these reports that considerable difference of opinion exists with regard to the accuracy of differential diagnosis and whether laparotomy should be done. In these recent publications Bothe and Pote, Braithwaite and Coleman were of the opinion that operation is definitely indicated, whereas Tilley, King and Aird were willing to defer operation, Aird "confidently" allowing the patient to go home.

In an attempt to settle this difference in opinion, the records of the 268 cases of acute mesenteric lymphadenitis observed at the Duke Hospital have been reviewed and compared with the records of 100 unselected cases of simple acute suppurative appendicitis treated during the same period. In addition, follow-up studies by letter or clinic visit were carried out in the group with mesenteric lymphadenitis. The data form the basis of this communication.

#### INCIDENCE

The comparative incidence of appendicitis and nonspecific mesenteric lymphadenitis has been indicated in the introduction. There were 99 males and 169 females with mesenteric lymphadenitis. Two

TABLE 1.—*Age Incidence*

Age, Yr.....	0 to 5	6 to 10	11 to 15	16 to 20	21 to 25	26 to 30	31 to 40	41 to 50	Over 50
Appendicitis, %.....	1.0	2.0	19.0	31.0	20.0	11.0	8.0	6.0	2.0
Mesenteric adenitis, %	2.3	12.8	30.4	37.2	11.6	3.8	1.5	0.4	0

hundred and fifty-five of the patients were white, 11 were Negro and 2 were Indian. Analysis by seasons was without significance. Occurrence by age was charted in table 1, which showed a comparative increase in mesenteric lymphadenitis in the younger age groups.

#### HISTORY

Only 7 per cent of patients with appendicitis had prior similar attacks whereas 47.4 per cent of patients with mesenteric lymphadenitis had one or more attacks of pain before the episode which caused hospitalization. Duration of symptoms at the time of hospitalization was about the same, as noted in table 2, except that the percentage of patients with symptoms for more than seventy-two hours was greater in the group with mesenteric lymphadenitis.

Abdominal pain was the first and predominant symptom in 96 per cent of patients with appendicitis and in 90 per cent of patients with mesenteric lymphadenitis. The pain began in the right lower quadrant in 39.5 per cent with mesenteric lymphadenitis and in 19 per cent

with appendicitis. In the cases of mesenteric lymphadenitis the pain at onset was periumbilical in 31.9 per cent, compared with 14 per cent in the cases of appendicitis. Epigastric pain was the first noted in 22 per cent of patients with appendicitis and 14.2 per cent with mesenteric lymphadenitis. Generalized abdominal pain occurred first in 23 per cent and pain in both lower quadrants in 14 per cent of the patients with appendicitis, whereas these were rarely the site of onset of pain in mesenteric lymphadenitis. When the pain did not begin in the right lower quadrant, it later localized there in 88 per cent of the patients with appendicitis and 66 per cent of those with mesenteric lymphadenitis.

The character of pain in both groups varied so markedly as to prohibit detailed analysis. It was noted, however, that in cases of appendicitis the pain usually persisted, frequently becoming gradually more severe, whereas with mesenteric lymphadenitis the pain was intermittent and usually colicky when present, with periods of complete freedom from it. The latter type was noted in 28.7 per cent of

TABLE 2.—*Duration of Symptoms*

Duration, Hr.....	6	6 to 12	12 to 24	24 to 48	48 to 72	Over 72
Appendicitis, %.....	5.0	16.0	28.0	38.0	12.0	1.0
Mesenteric adenitis, %.....	0.5	15.8	27.1	22.3	12.1	16.2

the patients with mesenteric lymphadenitis and in only 4 per cent of those with appendicitis.

Nausea and vomiting were slightly more frequent in cases of appendicitis. Diarrhea or constipation occurred in almost exactly the same percentage of patients in each group; 11 per cent had diarrhea, and 6 per cent had constipation. Of the patients with mesenteric lymphadenitis, 54.5 per cent gave a history of a recent or persistent infection of the upper respiratory tract or showed signs of such infection on examination.

#### EXAMINATION

In general, the routine physical examination revealed nothing remarkable, and the findings of principal interest pertained to the abdomen. Tenderness in the right lower quadrant was present in 99 per cent of the patients with appendicitis and in 89.6 per cent with mesenteric lymphadenitis. With appendicitis, tenderness was also present in the left lower quadrant in 30 per cent, the right upper quadrant in 2 per cent and the epigastrium in 1 per cent and was generalized in 1 per cent. Conversely, in patients with mesenteric lymphadenitis there was tenderness in the left lower quadrant alone or in addition in 15.2 per cent, the right upper quadrant in 3.1 per cent and

the epigastrium in 2.2 per cent. In this group it was generalized in 10.4 per cent. The tenderness was more frequently and definitely localized in the right lower quadrant in cases of appendicitis. Although not obvious from the records, the tenderness in mesenteric lymphadenitis, when carefully outlined, was frequently found to extend along the root of the mesentery of the small bowel, i. e., from the right lower quadrant obliquely upward and to the left across the umbilicus. A comparison of signs of peritoneal irritation showed a decided difference. Local rebound tenderness was present in 76 per cent with appendicitis and 35.8 per cent with mesenteric lymphadenitis, referred rebound tenderness was found in 62 per cent with appendicitis and 27.1 per cent with mesenteric lymphadenitis and muscle spasm occurred in 60 per cent with appendicitis and 35.4 per cent with mesenteric lymphadenitis. Tenderness by rectal examination was almost exactly the same (69 and 68.7 per cent).

TABLE 3.—*Temperature on the Patient's Admission to the Hospital*

Temperature, Degrees, F.....	96.8 to 99.5	99.6 to 100.4	100.5 to 101.3	101.4 to 102.2	102.3 to 103.1	Over 103.1
Appendicitis, %.....	48	28	17	4	3	0
Mesenteric adenitis, %	67	15	12	3	1	2

TABLE 4.—*White Blood Cell Counts*

Count.....	4,000-10,000	10,100-12,500	12,600-15,000	15,100-20,000	20,100-25,000	25,100-30,000
Appendicitis, %.....	22	19	21	27	8	3
Mesenteric adenitis, %	49	25	17	7	2	0

The rectal temperature at the time of the patients' admission to the hospital was generally higher in those with appendicitis (table 3). A similar and more pronounced trend was noted in the white blood cell counts (table 4).

#### PREOPERATIVE DIAGNOSIS

Of the 268 patients, 80 (30 per cent) were given a preoperative diagnosis of mesenteric lymphadenitis. For 73 of the 268 patients mesenteric lymphadenitis was listed in the differential diagnosis but not thought to be most likely, and for the remaining 115 patients mesenteric lymphadenitis was not mentioned. The most frequent preoperative diagnosis was appendicitis.

#### OPERATIVE FINDINGS

In all the patients with mesenteric lymphadenitis in this series, the appendix was grossly normal at operation. The lymphadenitis was described as slight in 48, moderate in 169 and marked in 51. Consider-



able variation in interpretation of the degree of lymphadenitis was apparent. In the operative notes, associated conditions described were as follows: salpingitis, 2 cases; ileitis, 4 cases; acute Meckel's diverticulitis, 1 case and ureteral stone, 1 case. In all cases the appendix was removed.

#### PATHOLOGIC PROCESS

No lymph nodes were removed for histologic examination. In the case mentioned previously the impression of acute Meckel's diverticulitis was confirmed. The appendixes were normal pathologically, with the following exceptions: Acute appendicitis was present in 15 cases, subacute appendicitis in 6, chronic appendicitis in 6, fecalith in appendix in 7, obliterated lumen of appendix in 10, pinworms in appendix in 19, lymphoplasia of appendix in 5 and periappendicitis in 3.

#### POSTOPERATIVE COURSE

Fifty-one patients were febrile after operation. Fifteen had a temperature as high as 39 C. (102.2 F.) which was present for more than one day, and 9 had a sustained temperature over 39 C. The cause was an infection of the upper respiratory tract in 7, pneumonia in 2, bronchitis in 2 and pyelitis in 1. No cause other than the abdominal condition was demonstrable in the others. Four patients had severe nausea and vomiting postoperatively, and diarrhea developed in 1. There was infection of the wound in 1 case and parotitis in another, and in 1 case measles developed. One patient had transitory hematuria postoperatively, which could not be explained.

*Follow-up Data.*—The present status of 154 of the 268 patients was determined. One had been killed in an accident, and 1 died from an unknown cause. Two patients died of intestinal obstruction, 1 at this hospital and 1 elsewhere. Five other patients were readmitted because of intestinal obstruction, which occurred on two separate occasions in 3 of these.

One hundred and eighteen patients had remained perfectly well after operation, whereas 27, or 17.5 per cent, of the group followed had a recurrence of their pain. The recurrent pain was like that which was present prior to operation. Instances of incisional sensitiveness or menstrual disorder were eliminated as carefully as possible. The number of attacks averaged two or three. These persisted for an hour to several days, but most lasted twelve to eighteen hours. The patients usually felt that their subsequent attacks were less severe, but the majority had residual tenderness for several days. No definite etiologic or precipitating factors could be ascertained by questioning.

## COMMENT

The etiology of acute nonspecific mesenteric lymphadenitis remains doubtful, but it is felt that the enlarged lymph nodes probably represent reaction to injurious agents, either bacteria, viruses or their toxins, which originate in the appendix or ileum. The parasites which are occasionally found may provide a point of entry for these agents by mucosal injury.

Patients who had pathologic signs of inflammation in the appendix possibly should not be described as having mesenteric lymphadenitis, as the symptoms and signs were undoubtedly due to the appendical changes in many cases. The inclusion was deliberately made, however, as it is thought that definite pathologic changes would be found much more frequently if opportunity were available for more thorough abdominal exploration and such studies as histologic examination of the ileal wall.

Mesenteric lymphadenitis is an operative diagnosis and can be strongly suspected preoperatively, but a preoperative diagnosis of mesenteric lymphadenitis should necessitate operation as readily as a preoperative diagnosis of acute appendicitis. Nearly half of the reported group of patients with mesenteric lymphadenitis were under 15 years of age, and diagnosis of appendicitis is notoriously treacherous in children because of atypical symptomatology. Actually, atypical appendicitis is common in all age groups, as shown in the summary of 500 cases from this hospital by Gardner and Sapp.<sup>15</sup> Therefore, as acute appendicitis may frequently present atypical manifestations and as mesenteric lymphadenitis may mimic appendicitis in any of its forms, operation is essential to avoid overlooking an acutely inflamed appendix which should be removed.

In an analysis of a large series of cases, statistical differences in the occurrence of symptoms and signs will be noted, yet no single examination or group of findings is adequate to differentiate accurately between acute mesenteric lymphadenitis and acute appendicitis in the individual patient. The morbidity and mortality of simple appendectomy are now so low that the removal of ten or more normal appendixes, with the finding of mesenteric lymphadenitis, is more justifiable than permitting one appendix to perforate, with the resultant complications. In the rare instance in which intercurrent disease or other factors contraindicate operation, conservative treatment of suspected mesenteric lymphadenitis may be necessary. Infrequently the symptoms and signs may suggest mesenteric lymphadenitis and be so mild that the patient is held under careful observation.

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15. Gardner, C. E., Jr., and Sapp, C. J.: Atypical Features in Manifestations of Acutely Inflamed, Nonruptured Appendix, *Am. J. Surg.* **57**:477-482 (Sept) 1942.

## SUMMARY

Nonspecific mesenteric lymphadenitis is a symptom complex characterized by abdominal pain and tenderness. Many of the patients have a history of prior attacks of pain, and about half have an infection of the upper respiratory tract. The pain usually begins in the right lower quadrant, epigastrium or periumbilical region, and when it does not begin in the right lower quadrant it localizes there in 66 per cent of the patients. It frequently comes in paroxysms, with intervals of complete relief. Tenderness is usually present in the right lower quadrant, but signs of peritoneal irritation occur in only about one third of the cases. The temperature and the white blood cell count may or may not be increased. Of 154 patients followed in this series, 17.5 per cent had recurrence of the same pain. Operation, with removal of the appendix, is strongly advised, as an accurate differential diagnosis between mesenteric lymphadenitis and acute appendicitis cannot be made.

# SEVERE INTERFERENCE WITH BILE FLOW IN PRIMARY HEPATITIS

Its Significance in the Differential Diagnosis of Jaundice

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**P**RONOUNCED interference with the bile flow is, as a rule, characteristic of extrahepatic biliary obstruction, usually of mechanical character, caused by stones, strictures and tumors. Hence surgical intervention is usually considered in cases of such nature. Only rarely is an intrahepatic mechanical obstruction of the larger bile ducts encountered. In contrast to earlier belief, however, interference with bile flow is met not uncommonly in cases of primary hepatitis in the acute or chronic stage. This interference may present complete biliary obstruction characterized by absence of bile from the duodenum and consequent lack of urobilinogen in the urine. In cases of primary hepatitis the phenomenon has been called intrahepatic biliary obstruction, and it has been the subject of several descriptive analyses.<sup>1</sup> Various hypotheses as to the pathogenesis of this phenomenon have been presented.<sup>2</sup> Recently, Watson and Hoffbauer<sup>3</sup> described cases of temporary exclusion of bile from the duodenum in instances of infectious hepatitis in which the damage to the hepatic cells was either subsiding or absent. They called this condition cholangiolitic hepatitis. They assumed damage of the cholangioles, not demonstrable morphologically, which

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1. (a) Lichtman, S. S.: *Diseases of the Liver, Gallbladder and Bile Ducts*, Philadelphia, Lea & Febiger, 1942. (b) Steigmann, F., and Popper, H.: Intrahepatic Obstructive Jaundice, *Gastroenterology* 1:645 (July) 1943.

2. (a) Eppinger, H.: *Die Leberkrankheiten*, Vienna, Julius Springer, 1937. (b) Popper, H.: Seroe Hepatitis, *Wien. klin. Wchnschr.* 49:207 (Feb. 14) 1936.

3. Watson, C. J., and Hoffbauer, F. W.: The Problem of Prolonged Hepatitis with Particular Reference to the Cholangiolitic Type and the Development of Cholangiolitic Cirrhosis of the Liver, *Ann. Int. Med.* 25:195 (Aug.) 1946.

may become chronic and which was considered responsible for the backflow of bile into the blood. In subsequent studies<sup>4</sup> they considered this cholangiolar dysfunction the main basis of hepatic jaundice.

In addition to the relatively small number of cases in which prolonged complete biliary obstruction is evidenced by the absence of urobilinogen from the urine, there is a larger group in which some function tests of interference with bile flow reveal pathologic conditions. Some interference with the bile flow is found in every case of regurgitation jaundice, i. e., medical or surgical. This is indicated by the increase of the direct serum bilirubin. However, severe interference with the bile flow as usually noted in cases of extrahepatic biliary obstruction is indicated by increase of the serum alkaline phosphatase and the total serum cholesterol in addition to absence of urobilinogen from the urine and stool. This definition may appear arbitrary, but it permits a workable diagnostic criterion. In general, then, in the presence of jaundice, increase of the serum alkaline phosphatase in the absence of pathologic bone changes, increase of the total serum cholesterol level, reduced urinary urobilinogen and decreased fecal urobilinogen must be considered as evidence of severe interference with bile flow. These findings may be temporary or prolonged. Such cases represent a diagnostic problem because of the difficulty in differentiating them from surgical conditions in which damage to hepatic cells is found in addition to signs of severe interference with bile flow.

In this paper an attempt is made (1) to establish the incidence of laboratory evidence of severe interference with bile flow in primary hepatitis; (2) to analyze the results of liver function tests in cases of this disease; (3) to compare them with the results in a group of cases of extrahepatic biliary obstruction observed during the same period; (4) to establish the duration of this phenomenon; (5) to correlate it with the different types of hepatitis, and (6) to discuss the pathogenesis of this condition based on biopsy studies.

#### MATERIAL AND METHOD

The material of this study consists of 65 cases of proved primary hepatitis (infectious or toxic) and cirrhosis which have been examined in the past five years and in which the diagnosis was established with reasonable certainty by either subsequent course, biopsy, operation or necropsy. The results of the liver function tests on the patients' admission to the hospital were the ones taken into consideration. The presence of positive results in at least two tests for damage to hepatic cells (cephalin-cholesterol flocculation, thymol turbidity, albumin-globulin ratio, cholesterol-cholesterol ester ratio, hippuric acid synthesis, plasma

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4. Watson, C. J., and Hoffbauer, F. W.: Liver Function in Hepatitis, *Ann. Int. Med.* **26**:813 (June) 1947.

vitamin A, nonprotein nitrogen and increased urinary urobilinogen)<sup>5</sup> was considered necessary for the assumption of impaired function of the hepatic cells. The second requirement in this group of cases was a positive result of at least one of the tests indicative of severe interference with bile flow (decrease of urobilinogen in feces and urine and increased serum cholesterol and serum alkaline phosphatase).

As signs of severe interference with bile flow were taken (1) a serum alkaline phosphatase level of over 15 Bodansky units, (2) a total serum cholesterol level of over 300 mg. per hundred cubic centimeters, (3) less than 1.0 mg. of urobilinogen in the urine in a twenty-four hour specimen<sup>6</sup> or less than  $\frac{1}{2}$  unit in a two hour specimen<sup>7</sup> and (4) less than 10 mg. of urobilinogen in 100 Gm. of stool.<sup>8</sup>

A phosphatase level of over 15 Bodansky units was taken as an indication of severe interference with bile flow because pathologic levels of between 4 to 15 units are too commonly found in all types of hepatitis. Obviously, a phosphatase level higher than 15 Bodansky units may be due to causes other than biliary or hepatic, but in the presence of jaundice such other causes are rarely to be considered. Similar considerations hold true also for the selection of a total serum cholesterol level of 300 mg. per hundred cubic centimeters.

In 2 cases of this series only one of the tests for impairment of hepatic function gave a positive reaction, and in 1 case no impairment was noted. In all 3 of them results of tests for severe interference with bile flow were positive. Their medical nature, however, was indicated by their history and confirmed by the subsequent course.

The entire series of 65 cases was contrasted with 46 cases in which similar results of function tests were obtained and which were observed during the same period but which proved to be cases of surgical jaundice.

## RESULTS

*Incidence.*—During the period in which we studied the 65 cases of medical jaundice in which severe interference with bile flow was revealed at the time of admission to the hospital, 228 cases of primary hepatitis were observed. Accordingly, 28.5 per cent of cases of medical jaundice revealed severe interference with bile flow.

*Analysis of Tests.*—In the 65 cases of this group, usually three or four of the tests for damage to hepatic cells gave positive results

5. The pathologic levels in the various tests and the method used are described in another paper (Popper, H., and Steigmann, F.: Laboratory Tests in the Differential Diagnosis of Jaundice, *Ann. Int. Med.* 29:469 [Sept.] 1948).

6. Watson, C. J.: Studies of Urobilinogen: I. An Improved Method for the Quantitative Estimation of Urobilinogen in Urine and Feces, *Am. J. Clin. Path.* 6:458 (Sept.) 1936.

7. Watson, C. J.; Schwartz, S.; Sborov, V., and Bertie, E.: A Simple Method for the Quantitative Recording of the Ehrlich Reaction as Carried Out with Urine and Feces, *Am. J. Clin. Path.* 14:605 (Dec.) 1944.

8. Steigmann, F., and Dyniewicz, J. G.: Studies of Urobilinogen: The Daily Urobilinogen Excretion in Urine and Feces in Health and Disease; An Evaluation of Watson's and Sparkman's Method, *Gastroenterology* 1:743 (Aug.) 1943.

(fig. 1). The number of instances in which each of the tests indicated a pathologic condition is given in table 1. It appears from it that the cephalin-cholesterol flocculation and thymol turbidity tests, as well as the albumin-globulin ratio, most often indicated a pathologic condition, whereas the cholesterol-cholesterol ester ratio was significantly lowered in about half of the cases. In a few cases with signs of severe interference with the bile flow the urinary urobilinogen level appeared high. In them, however, the interference was manifested only by increase in the phosphatase and/or the total cholesterol.

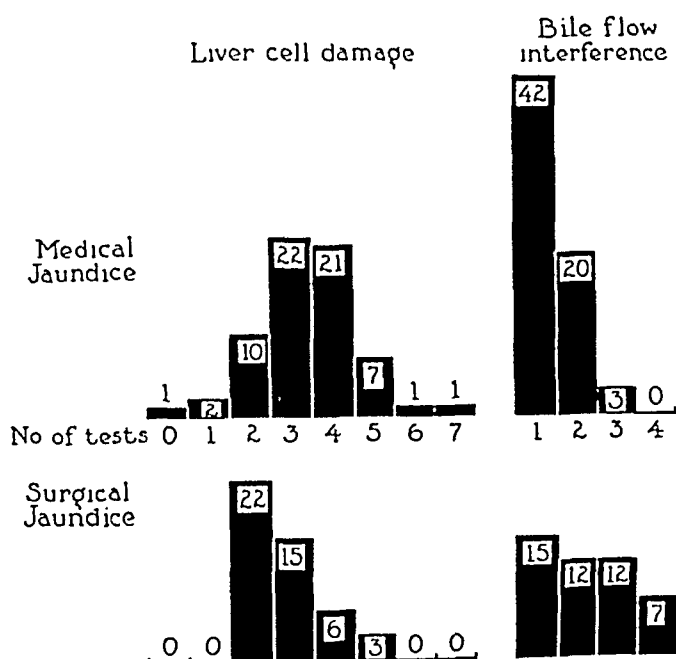


Fig. 1.—Number of patients (indicated by black column) in whom a given number of liver function tests elicited a positive reaction.

TABLE 1.—Results of Tests for Impairment of Hepatic Function in the Presence of Severe Interference with Bile Flow and Damage to Hepatic Cells

Type of Test *	Positive Results, Percentage	
	Medical Jaundice	Surgical Jaundice
Cephalin-cholesterol flocculation.....	87.6	28.0
Thymol turbidity.....	72.3	54.3
Albumin-globulin ratio.....	70.7	76.0
Cholesterol-cholesterol ester ratio.....	52.3	58.6
Hippuric acid excretion.....	21.5	28.2
Nonprotein nitrogen.....	15.3	21.7
Increased urinary urobilinogen.....	7.7	6.5

\* The tests for plasma vitamin A and for retention of sulfobromophthalein, which were done only on a small number of patients, were not listed in this table.

In the great majority of cases only one of the tests indicating severe interference with bile flow gave a positive result, as seen in table 2. In two thirds of the cases absence of urinary urobilinogen was the determining factor in grouping them into this category, and in only one third was an appreciable increase in the phosphatase or total cholesterol responsible.

*Comparison with Cases of Surgical Jaundice.*—During the period in which the 65 cases of primary hepatitis or cirrhosis with severe interference with bile flow were observed, 46 cases of surgical jaundice were also studied in which the laboratory tests presented evidence of damage to hepatic cells in addition to severe interference with bile flow. Since these cases, at least from the laboratory standpoint, simulate the cases of primary hepatitis discussed here, they are contrasted in figure 1 and tables 1 and 2.

TABLE 2.—*Results of Tests for Severe Interference with Bile Flow in Cases in Which Both Damage to Hepatic Cells and Interference with Bile Flow Were Present*

Type of Test *	Positive Results, Percentage	
	Medical Jaundice	Surgical Jaundice
Absence of urinary urobilinogen.....	69.2	79.2
Alkaline phosphatase.....	29.2	69.5
Total cholesterol.....	15.3	50.0

\* Fecal urobilinogen was not determined in all cases.

It is apparent that the number of tests indicating damage to hepatic cells is, on the average, smaller in the surgical group, although only cases in which at least two tests gave positive results were considered. As expected from reports in the literature<sup>9</sup> and our previous observations, the cephalin-cholesterol flocculation reaction was positive in only a relatively small number of cases of surgical jaundice and the thymol turbidity reaction in about half, while the other tests gave almost identical results. The difference in the number of positive reactions is therefore primarily due to the difference in the results of the first two tests.

Of the tests for severe interference with bile flow, a much higher number, on the average, elicited positive reactions among the surgical cases. This was primarily due to the high incidence of markedly increased alkaline phosphatase and total cholesterol levels.

9. Hanger, F. M.: Serologic Differentiation of Obstructive from Hepatogenous Jaundice by Flocculation of Cephalin Cholesterol Emulsion, *J. Clin. Investigation* 18:261 (May) 1939. Rosenberg, D. H.: The Cephalin-Cholesterol Flocculation Test in Cases of Disease of the Liver, *Arch. Surg.* 43:231 (Aug.) 1941.



*Type of Hepatitis.*—The cases of primary hepatitis with marked interference in bile flow discussed in this paper can be divided etiologically into cases of homologous serum jaundice, infectious (viral) hepatitis, toxic hepatitis and cirrhosis. Figure 2 indicates also the additional cases of primary hepatitis without severe interference in bile flow observed during the same period. The highest incidence of this phenomenon was found in the group of cases of homologous

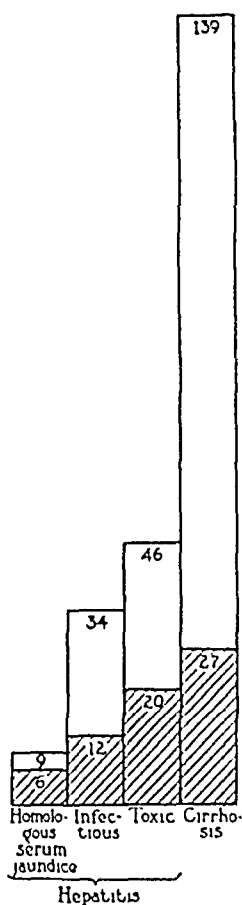


Fig. 2.—Incidence of marked interference with bile flow in the various types of hepatitis and in cirrhosis indicated by the cross-hatched columns. The total number of cases observed is indicated by the entire column.

serum jaundice (66.6 per cent). The next highest incidence was seen in cases of toxic hepatitis (43.5 per cent). It occurred in 35.3 per cent of cases of infectious hepatitis and in 19.3 per cent of the observed cases of cirrhosis.

*Duration of Interference with Bile Flow.*—The duration was not established in the majority of cases because daily follow-up examinations were not available. In a relatively small number of cases daily deter-

minations of urobilinogen were made which indicated the length of time during which urobilinogen was absent from the urine. In 9 of the 65 cases absence of urobilinogen from the urine persisted for three to ten days, whereas in 12 cases it persisted for over ten days. In 1 case each the phenomenon was observed for thirty-three, thirty-seven and forty-one days.

*Histologic Observations.*—Biopsies of material from the liver<sup>10</sup>—needle aspiration or surgical—were performed in some cases at a time when interference with the bile flow existed. In contrast to expectations based on a few scattered observations in the literature<sup>11</sup> as well as on experience from our own old material,<sup>1b</sup> no characteristic morphologic changes were found which differentiated the cases of primary hepatitis with severe interference in bile flow from those without it. Previously, inflammatory changes in the portal triads associated with portal fibrosis or proliferation of the bile ducts were considered responsible for the interference with the bile flow by causing compression or actual interruption of the smallest bile ducts. In some of the patients with primary hepatitis and severe interference with the bile flow, extensive infiltration by round cells and occasionally also by polymorphonuclear cells was found in the periportal fields, presenting the characteristic picture of a subacute or chronic perilymphangitis. The cellular exudate surrounded the septal bile ducts (fig. 3A). However, similar or even more extensive changes were found in cases of primary hepatitis without laboratory evidence of severe interference with bile flow (fig. 3B). Moreover, in some of the cases of acute hepatitis, even in those in which there was long duration of interference with bile flow, the described inflammatory changes were absent and the portal triads revealed no morphologically recognizable aberration from the normal. The hepatic cells were, however, loaded with bile pigment, and the bile capillaries, especially, in the center of the lobules were dilated and filled with casts (fig. 3C). Only in a few cases of cirrhosis was there a morphologic picture which could explain the marked interference with bile flow. Dense fibrous connective tissue encircled the smallest bile ducts and seemed to compress them, whereas the nearby bile capillaries in the periphery of the lobules appeared maximally dilated. This picture appeared to be the result of an obstruction (fig. 3D).

10. The aspiration biopsies were performed by Dr. D. D. Kozoll and Dr. I. Stein Jr.

11. Hanger, F. M., and Guttman, A. B.: Postarsphenamine Jaundice Apparently Due to Obstruction of Intrahepatic Bile Tract, *J. A. M. A.* **115**:263 (July 27) 1940. Popper.<sup>2b</sup>

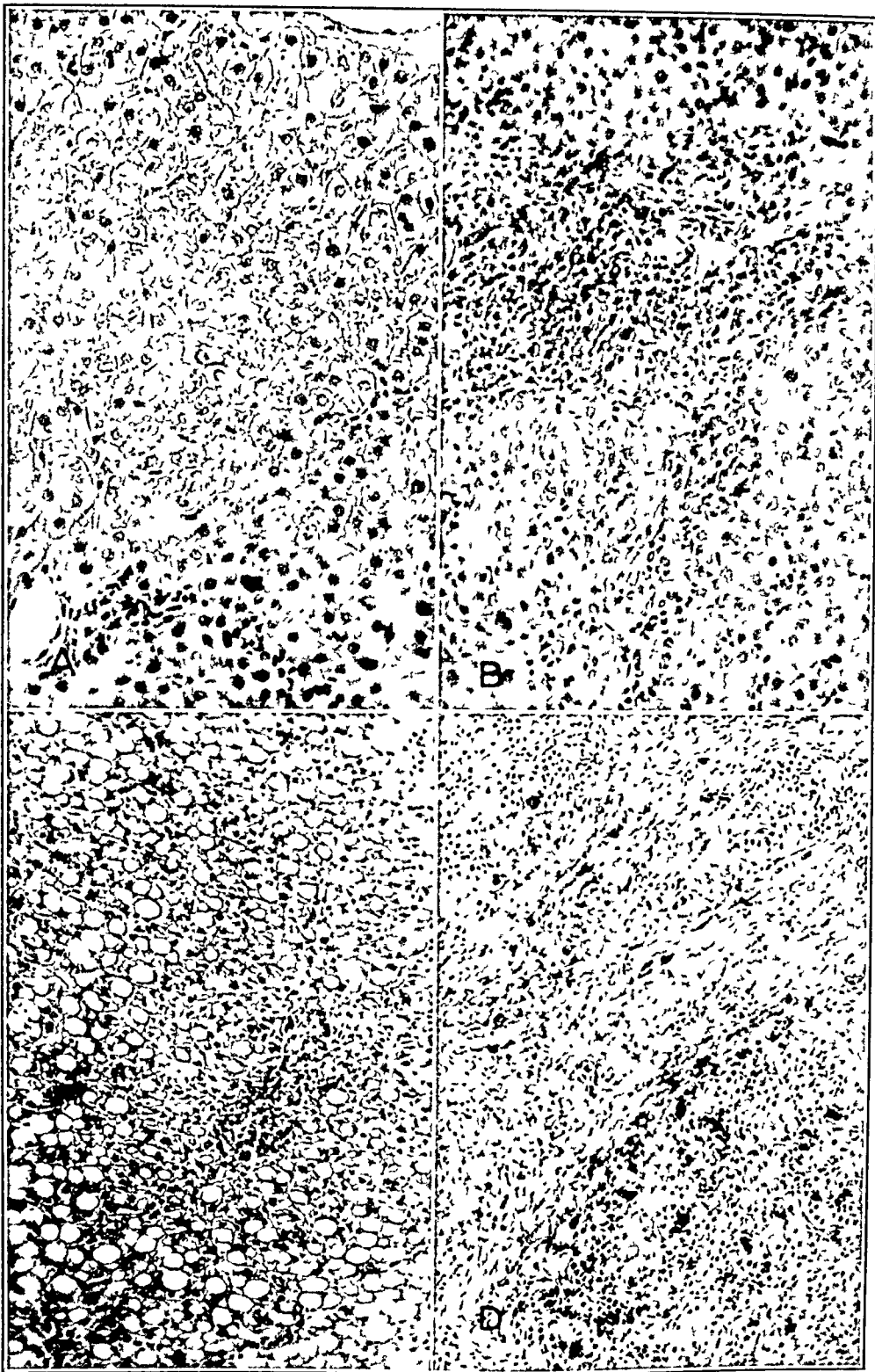


Fig. 3.—Photomicrographs of specimens of liver. *A*, acute infectious hepatitis associated with marked interference with bile flow. Moderate damage to hepatic cells, bile pigment in cells and bile casts in bile capillaries are revealed; round cellular exudate is found around septal bile ducts in a small portal triad. *B*, subacute infectious hepatitis without great interference with bile flow. There is considerable damage to hepatic cells, with regeneration. There is dense round cellular and histiocytic infiltration of the portal triads radiating into the parenchyma along septal bile ducts. *C*, toxic hepatitis of the fatty type associated with marked interference with bile flow. Much bile pigment is seen in hepatic cells. The dilated bile capillaries contain bile casts; the periportal fields are not infiltrated. *D*, portal cirrhosis associated with great interference with bile flow. The septal bile ducts in the wide connective tissue trabeculae are encircled by dense collagenous fibers, whereas the bile capillaries on the periphery of the nodules are dilated and filled with bile casts.

## REPORT OF CASES

CASE 1.—A 23 year old white woman entered the hospital because of fever, coryza, headache, malaise, anorexia, nausea and vomiting. These symptoms began about two weeks after a prophylactic injection of influenza vaccine. Two and a half weeks before her admission to the hospital she noticed that her urine had become dark and her stools light, and shortly thereafter she became aware of a yellowish discoloration of her skin. The jaundice appeared to increase in severity, and swelling of her legs and dyspnea on exertion developed. The patient denied taking any medication or having been exposed to any industrial hazards. On admission she was severely jaundiced but well nourished. The abdomen was slightly distended, the liver was palpable 2 cm. below the costal margin and there was pitting edema of the legs. The urine contained bilirubin but no urobilinogen. The hemoglobin content was 55 per cent, with a red blood cell count of 3,920,000. The white blood cell count was 6,450, with 75 per cent polymorphonuclear cells, 15 per cent lymphocytes and 10 per cent monocytes. The erythrocytes showed a tendency to macrocytosis. The nonprotein nitrogen content was 25 mg. per hundred cubic centimeters, the total serum cholesterol 112 mg., with 10.7 per cent cholesterol esters, the serum alkaline phosphatase 5.6 Bodansky units, the icterus index 112, the thymol turbidity 8.6 units, the cephalin-cholesterol flocculation 4 plus and the albumin-globulin ratio 2.8:1.5. A diagnosis of infectious hepatitis—possibly homologous serum jaundice—was made. The patient was treated with a 4,000 calorie diet, high in carbohydrates and protein; she also received a liver preparation intravenously. Repeated examinations of urine showed bilirubin but no urobilinogen. Not until the twenty-third day after admission did a trace of urobilinogen appear in the urine. The patient had a stormy course; her abdomen became more distended, ascites developed and edema of the legs increased. However, after repeated blood transfusions and administration of vitamin preparations and amino acids she continued to improve. After thirty days repeat liver function tests showed the cephalin-cholesterol flocculation to be 4 plus, the thymol turbidity 11.6 and the total serum cholesterol 123. The cholesterol esters had increased to 55 per cent. The total serum protein, however, was still low, and the albumin-globulin ratio was reversed to 1.6:3.0; the alkaline serum phosphatase was 6.9 units, and the urine contained 3 units of urobilinogen. The patient continued to improve and left the hospital ninety-five days after admission.

CASE 2.—A 40 year old man entered the hospital because of jaundice of one week's duration. He had no pain but only mild nausea, weakness and slight pruritus. The stools had been clay colored for four or five days. He had been taking about 2 quarts (2,000 cc.) of beer daily for over twenty years. There had been no exposure to any hepatotoxic drugs or industrial hazards. He denied having received blood or other injections in recent months. On admission he appeared well nourished but jaundiced. The abdomen was protuberant, with the liver palpable 5 fingerbreadths, and the spleen 2 fingerbreadths below the costal margin. Ascites was present. Spider nevi were seen over the face and trunk. The urine contained bilirubin but no urobilinogen. The hemoglobin content was 67 per cent, with a red blood cell count of 3,560,000. The white blood cell count was 5,500, with 76 per cent polymorphonuclear cells, 10 per cent lymphocytes and 14 per cent monocytes; target cells were noted. The cephalin-cholesterol flocculation was 4 plus. The thymol turbidity test showed 6.4 units. The total

serum cholesterol was 475 mg. per hundred cubic centimeters, with 21 per cent cholesterol esters. The serum alkaline phosphatase was 11 Bodansky units. The albumin-globulin ratio was 3.0:3.0. A diagnosis of acute hepatic damage with intrahepatic obstruction in a patient with cirrhosis was made. The patient was put on a liver regimen, and urinary follow-up studies were made daily. On the twenty-fourth day urobilinogen appeared in the urine (2.59 mg. in twenty-four hours). At this time the cephalin-cholesterol flocculation was 4 plus and the thymol turbidity 8.6 units. The total serum cholesterol had dropped to 350 mg. per hundred cubic centimeters, the cholesterol esters had risen to 71 per cent, the serum alkaline phosphatase was 8.9 Bodansky units and the albumin-globulin ratio was 2.7:3.9. The patient improved slowly and was released from the hospital five weeks after admission.

CASE 3.—A 45 year old Negro woman entered the hospital because of anorexia, nausea, weakness and pain in the epigastrium of two weeks' duration and also jaundice and light stools for one week. Similar epigastric pain with nausea and vomiting but without jaundice had occurred two years before when she was told that her gallbladder was diseased. Since then she had occasional epigastric distress and nausea whenever she ate greasy or fried foods. There was no history indicating exposure to hepatotoxic drugs or of having received injections of any kind or blood products.

On her admission to the hospital she appeared icteric but was well developed and well nourished. Her abdomen was flat and soft, with slight tenderness in the right upper quadrant. No masses were palpable. A diagnosis of obstructive jaundice due to disease of the gallbladder was made, but the possibility of hepatitis was also considered. The urine contained bilirubin but no urobilinogen. The nonprotein nitrogen was 25 mg. per hundred cubic centimeters; the cephalin-cholesterol flocculation was 3 plus; the thymol turbidity was 13.2 units; the icterus index was 151; the albumin-globulin ratio was 2.8:2.8; the serum alkaline phosphatase was 3.9 Bodansky units, and the total serum cholesterol was 253 mg. per hundred cubic centimeters. Hematologic examination revealed slight anemia and macrocytosis, with a white blood cell count of 9,150 and 75 per cent polymorphonuclear cells. Because of the absence of urobilinogen from the urine and the rising icterus index (151 to 174) and because of her history, she was transferred to a surgical ward for an exploratory operation. At laparotomy the liver was found to be small and hard; the gallbladder and the common duct were not distended, and no stones were found anywhere. The surgeon's impression was that the patient had a cirrhotic liver. The common duct was drained. After operation she had a stormy course but improved gradually, and nineteen days postoperatively the cephalin-cholesterol flocculation was 2 plus; the thymol turbidity 3.0 units; the icterus index 61; the albumin-globulin ratio 3.0:1.9; the alkaline serum phosphatase 3.0 Bodansky units; the total serum cholesterol 206 mg. per hundred cubic centimeters; the cholesterol esters 61 per cent; the urine urobilinogen 58.32 mg. in twenty-four hours, and the stool urobilinogen 59.2 mg. per hundred cubic centimeters. The patient left the hospital seven weeks after operation. Follow-up examination three months later showed an albumin-globulin ratio of 4.1:3.2; a total serum cholesterol level of 357, with 67 per cent cholesterol esters; a thymol turbidity of 8.6 units; a total bilirubin level of 1.6 mg. per hundred cubic centimeters; normal cephalin-cholesterol flocculation, and normal stool and urine urobilinogen levels.

## COMMENT

The occurrence of severe interference with bile flow in medical jaundice is obviously of importance in the differential diagnosis, because it may suggest an extrahepatic mechanical origin of the jaundice, which therefore would require operation. A survey of a large number of cases of jaundice due to established primary hepatitis or cirrhosis revealed that in such cases severe interference with bile flow is not uncommon. It occurred approximately in one fourth of the cases if one took the first complete laboratory examination into account. At times it was rather persistent, although the material presented here does not permit statements as to the duration in most cases.

From the laboratory standpoint this group is almost identical with the large group of cases of surgical jaundice in which damage to hepatic cells is present. Obviously, clinical observation based on an exact history and clinical findings will often permit the differentiation. However, laboratory examinations are of some, though limited value. As a rule, more tests for damage to hepatic cells and less tests for severe interference with bile flow give positive results in the medical group. In the latter the reaction to the cephalin flocculation test is far more often positive, less so the reaction to the thymol turbidity test, whereas the other tests fail to show much difference in the results. On the other hand, the alkaline phosphatase is markedly increased (above 15 Bodansky units) and the total cholesterol is above 300 mg. per hundred cubic centimeters more often in the surgical cases than in the medical cases. On the average, therefore, severe interference with bile flow is less conspicuous in medical jaundice and impairment of hepatic function is less marked in surgical jaundice. In the individual case this relation is not always borne out, a fact which calls for alertness in the interpretation of the tests of function.

It is of considerable interest that the incidence of this phenomenon varies in the different types of hepatitis. Recently, based on morphologic examination, the difference between infectious (viral) and toxic hepatitis (including various known and unknown toxic agents) has been emphasized.<sup>12</sup> If the cases of infectious hepatitis, including homologous serum jaundice, from our material are contrasted with those of toxic hepatitis, the incidence of severe interference with bile flow is about identical, namely 41.8 versus 43.5 per cent. However, if the patients with homologous serum jaundice are taken as a separate group, an unusually high incidence of severe interference with bile flow is found, if one is permitted to draw conclusions from this small group. In contrast,

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12. Popper, H., and Franklin, M.: *Differential Diagnosis of Hepatitis by Histologic and Functional Laboratory Methods*, J. A. M. A. **137**:230 (May 15) 1948.

the patients with infectious (viral) hepatitis, which is transmitted by the oral route, show this phenomenon less often than those with toxic hepatitis. This points to a difference between viral hepatitis and homologous serum jaundice,<sup>13</sup> which is in keeping with the observation that the latter is, as a rule, the more severe disease.<sup>14</sup> Obviously the presented breakdown of the cases is only suggestive and not established; previous exposure to blood products does not definitely prove homologous serum jaundice as a cause of the hepatitis. In the group of cases of infectious hepatitis, the diagnosis remains assumptive without demonstration of the virus or a clearcut epidemiologic background. In contrast to acute hepatitis, the phenomenon of severe interference with bile flow is far less common in cirrhosis with jaundice.

Little can be added to the understanding of the pathogenesis of this phenomenon except to withdraw statements previously made.<sup>1b</sup> Only in some cases of cirrhosis is a characteristic morphologic picture associated with the phenomenon, namely, when there is an encircling fibrosis obstructing the septal bile ducts. It apparently accounts for the cholestatic phase in cirrhosis. In acute hepatitis no characteristic morphologic changes can be associated with this phenomenon. A study of a larger number of cases did not confirm the previously made assumption that inflammatory changes in the periportal fields are responsible for it. At the present stage of our knowledge the explanation proposed by Watson and Hoffbauer,<sup>3</sup> namely, backflow of bile through anatomically unchanged cholangioles, can be accepted. Therefore one may be justified in the use of cholangiolitis as a descriptive term for this phenomenon.

It is questionable whether the higher incidence of severe interference with bile flow in the cases of homologous serum jaundice is an expression of a greater severity of the hepatitis in general or whether this disease is associated with a more marked involvement of the smallest bile ducts, cholangioles, than the other types of hepatitis. The second possibility might be explained by a greater affinity of the homologous serum virus for the cholangioles.

#### SUMMARY

Severe interference with bile flow as indicated by absence of urobilinogen from the urine and feces or markedly increased levels of serum alkaline phosphatase and total cholesterol was found in 28.5 per cent of cases of medical jaundice (primary hepatitis or cirrhosis).

13. Neefe, J. R.: Recent Advances in the Knowledge of "Virus Hepatitis," *M. Clin. North America* **30**:1407 (Nov.) 1946.

14. Lucke, B., and Mallory, T.: The Fulminant Form of Epidemic Hepatitis, *Am. J. Path.* **22**:867 (Sept.) 1946.

In order of decreasing incidence, this phenomenon was found in homologous serum jaundice, toxic hepatitis, infectious (viral) hepatitis and cirrhosis. In contrast to cases of surgical jaundice with damage to hepatic cells, tests indicated impairment of hepatic function more often and severe interference with bile flow less often in this group. The reaction to the cephalin-cholesterol flocculation test was far more often positive and the serum alkaline phosphatase and total cholesterol levels were less often markedly increased in the medical cases than in the surgical cases. A characteristic morphologic picture was present in some cases of cirrhosis, whereas in cases of acute hepatitis no correlation of severe interference in bile flow with anatomic changes was found. The importance of severe interference with bile flow (which is usually considered a characteristic of extrahepatic mechanical obstruction requiring surgical intervention) in the differential diagnosis of jaundice is emphasized.



## SUBMUCOUS LIPOMAS OF THE COLON

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AND

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FOR MANY years surgeons have been unusually interested in submucous lipomas of the gastrointestinal tract because of their rarity, bizarre symptomatology, difficulty of diagnosis and the good prognosis after resection.

Submucous lipomas have been found along the gastrointestinal tract from the hypopharynx to the rectum. When found in the stomach or small bowel they are usually small and rarely cause symptoms. The colon has the highest incidence of submucous lipomas, and here they sometimes become bulky and cause obstruction. Of the benign tumors of the intestinal tract, lipomas are second in frequency to adenomatous polyps.

The last survey of the literature was made by Gault and Kaplan<sup>1</sup> in 1941, and, including their cases, there were only 130 cases of submucous lipoma of the colon reported. Of these, 111 were clinical cases and the rest were found at autopsy. Since their summary, cases have been reported by Lazarus and Marks,<sup>2</sup> Browne and McHardy,<sup>3</sup> Saint,<sup>4</sup> Barnes and Barnes,<sup>5</sup> Cooper,<sup>6</sup> Moore,<sup>7</sup> Meigs,<sup>8</sup> Anderson and

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1. Gault, T., and Kaplan, P.: Submucous Lipoma of the Colon, *Am. J. Surg.* **53**:145 (July) 1941.

2. Lazarus, A., and Marks, M.: Submucous Lipomas of Colon with Special Reference to Acute and Chronic Intussusception, *Am. J. Surg.* **70**:114 (Oct.) 1945.

3. Browne, D. C., and McHardy, G.: Submucosal Colon Lipomas, *Clinics* **3**:622 (Oct.) 1944.

4. Saint, J. H.: Chronic Intussusception Due to Submucous Lipoma of Ascending Colon, *Am. J. Surg.* **58**:414 (Dec.) 1942.

5. Barnes, F. L., and Barnes, J. P.: Lipoma of the Colon, *South. Surgeon* **9**:853 (Dec.) 1940.

6. Cooper, H. G. N.: Intussusception in an Adult Due to a Lipoma, *Brit. M. J.* **1**:328 (Feb. 18) 1939.

*(Footnotes continued on next page)*

Fansler,<sup>9</sup> Clagett,<sup>10</sup> Didier,<sup>11</sup> Morton,<sup>12</sup> Spatolisano<sup>13</sup> and Pack and Booher.<sup>14</sup> Now about 155 cases have been reported in the literature.

Staemmler,<sup>15</sup> Comfort<sup>16</sup> and Kirshbaum<sup>17</sup> reported an incidence of submucous lipomas of the gastrointestinal tract at autopsy varying from 0.05 to 0.6 per cent. At this hospital Humphreys,<sup>18</sup> in reviewing 3,100 consecutive autopsies, found 23 cases in which there were submucous lipomas of the gastrointestinal tract—an incidence of 0.75 per cent. In 15 of this group the lipomas were located in the colon (65 per cent). In 9,648 autopsies of Comfort and Kirshbaum only 13 colonic submucous lipomas were found.

The surgical services of the Albert Merritt Billings Memorial Hospital of the University of Chicago Clinics in the past eleven years have had 7 cases of submucous lipomas of the colon. Six of these cases were of clinical significance, and in the other the lipoma was an incidental finding in a colon resected for carcinoma.<sup>19</sup> Since most reports in the literature have dealt with single cases, we feel that a series of this size is worth reviewing.

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7. Moore, E. C.: Obstructive Submucous Lipoma of the Cecum, California & West. Med. **60**:21 (Jan.) 1944.

8. Mallory, T. B.: Case Records of the Massachusetts General Hospital: Meig's Case 27042, New England J. Med. **224**:168 (Jan. 23) 1941.

9. Anderson and Fansler: Submucous Lipomas of the Rectum, Lancet **59**:4 (Jan.) 1939.

10. Clagett, O. T.: Lipoma of Cecum, Proc. Staff Meet., Mayo Clinic **14**:505 (Aug.) 1939.

11. Didier, R.: Submucous Lipomas of the Cecum, Two Cases, Arch. d. mal. de l'app. digestif. **28**:1070 (Dec.) 1938.

12. Morton: Submucous Lipomas of the Colon, Bull. Vancouver M. A. **16**:287 (July) 1940.

13. Spatolisano, B.: A Case of Lipoma of the Descending Colon, Rassegna internaz. clin. e terap. **27**:45, 1947.

14. Pack, G. T., and Booher, R. J.: Intussuscepting Submucous Lipoma of the Right Colon, S. Clin. North America **27**:361, 1947.

15. Staemmler, M.: Das Lipom in die Neubildungen des Darmes, Stuttgart, Ferdinand Enke, 1924, pt. 1, p. 273.

16. Comfort, M. W.: Submucous Lipoma of the Gastrointestinal Tract with a Report of Twenty-Eight Cases, Surg. Gynec. & Obst. **52**:108, 1931.

17. Kirshbaum, J. D.: Submucous Lipomas of the Intestinal Tract as a Cause for Intestinal Obstruction, Ann. Surg. **101**:734, 1935.

18. Humphreys, E.: Personal communication to the authors.

19. L. N. (case 7), a 60 year old housewife, was operated on Dec. 18, 1946, and a carcinoma of the ascending colon was found. As no distant metastasis had



Fig. 1.—Low power photomicrograph of the 15 cm. submucous lipoma found incidentally in the surgical specimen of case 7

occurred, a colectomy was performed on the right side. Examination of the specimen revealed a napkin ring constricting ulcerated carcinoma 14 cm above the ileocecal valve. As an incidental finding 2 cm above the ileocecal valve there was a soft fluctuant pedunculated mucosal nodule 15 cm in diameter. Microscopic examination of this showed it to be a benign nonulcerated submucosal lipoma (fig 1).

## REPORT OF CASES

CASE 1.<sup>20</sup>—A. G., a 59 year old housewife, was subjected to a Mikulicz resection of a portion of the sigmoid colon for adenocarcinoma in 1930. She was free of symptoms for nearly six years, when suddenly she had a moderate rectal hemorrhage. A year later, on Sept. 29, 1937, she came to the surgical clinic complaining of chronic constipation and of cramping pain in the lower abdominal region associated with nausea and small bloody stools during the past week.

Physical and laboratory examinations were essentially noncontributory. Fluoroscopy of the colon and roentgenograms demonstrated a polypoid tumor 5 by 7 cm. on the anterior wall of the transverse colon (fig. 2). This mass did not obstruct the lumen and was benign in the opinion of the examiner.

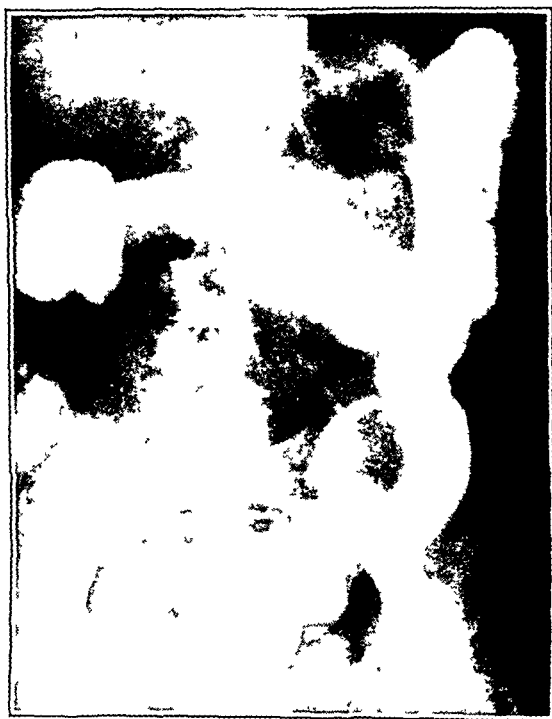


Fig. 2.—Roentgenogram of the colon in case 1, reported as showing a benign tumor mass 5 by 7 cm. arising from the inferior wall of the transverse colon and projecting into the lumen.

On Oct. 25, 1937, a laparotomy was performed and a submucous lipoma of the transverse colon was found. There was no evidence of recurrence of the sigmoid carcinoma. A Mikulicz resection of the tumor-containing segment of transverse colon was performed. The postoperative course was uneventful, and closure of the colostomy opening was carried out six weeks later.

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20. This case was reported by Dr. O. C. Julian in the April 1939 issue of Radiology.

The pathologic specimen consisted of a 5.5 cm. segment of colon containing a pedunculated soft yellow submucous tumor measuring 7.5 by 4.5 by 4.0 cm. The mass was freely movable beneath the intact mucosa and when cut was obviously a lobulated fatty tumor. Microscopic sections confirmed the diagnosis of lipoma (fig. 3).

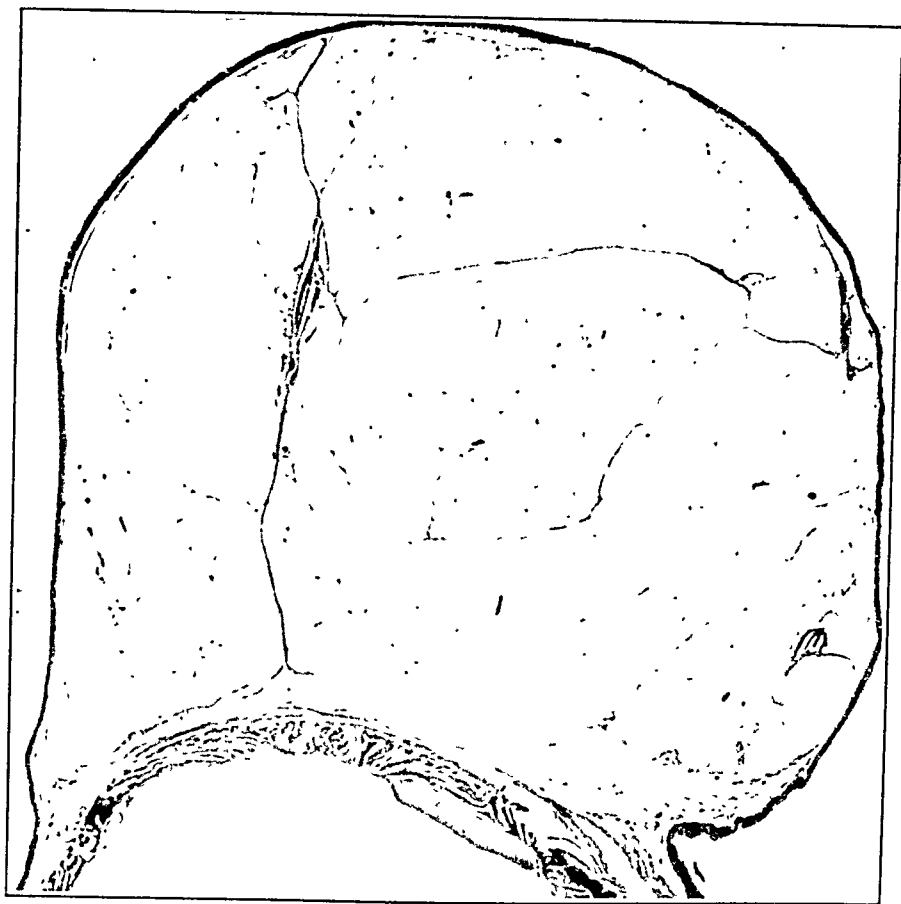


Fig. 3. —Low power photomicrograph of the resected colon and submucous lipoma in case 1.

CASE 2.—M. D., a 51 year old housewife, was seen in the surgical clinic on Nov. 6, 1940, complaining of cramping pain in the lower abdominal region increasing in frequency and severity for six weeks and relieved by bowel movements. She had lost 20 pounds (9.1 Kg.) of weight during this period and felt weak. She had noticed increasing difficulty in moving her bowels, and her stools were poorly formed and watery and contained a great deal of mucus.

Physical examination showed an anxious woman with evidence of recent loss of weight. A tender, smooth, movable mass 3 by 5 cm. was palpable at the level of the left iliac crest. Roentgenograms of the colon showed a 4 cm. polypoid mass almost filling the lumen of the distal part of the transverse colon. The

examiner was unable to differentiate between a benign or malignant lesion but favored the former. Mild anemia was present.

On Nov. 12, 1940, operation was performed and exploration revealed a mass in the region of the splenic flexure believed to be a papilloma or lipoma. A Mikulicz obstructive type of resection was carried out, a segment of the colon including the tumor being removed. Eleven weeks later the colostomy opening was closed.

Examination of the specimen revealed in the resected segment of colon a polypoid submucous tumor 3.5 cm. in diameter. The distal portion of the tumor, consisting of lobulated fat, was not covered by mucosa (fig. 4). Microscopic examination confirmed the gross impression of an ulcerated submucosal lipoma.

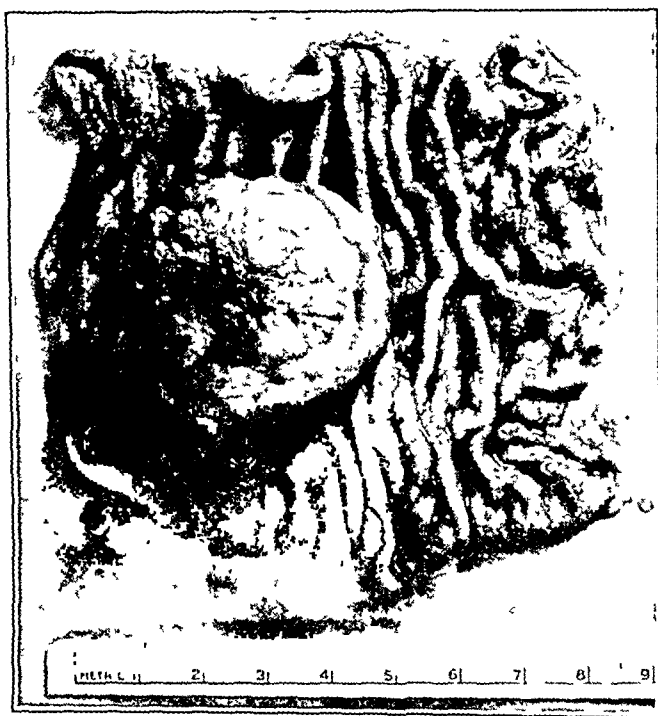


Fig. 4. —Photograph of the resected colon showing the polypoid submucous lipoma in case 2. The mucosa is absent over part of the surface exposing the lobulated fat of the tumor.

CASE 3.—S. T., a 40 year old housewife, was first seen on Nov. 20, 1942, in the gastrointestinal clinic complaining of attacks of cramping pain in the upper abdominal area present for five to seven years and relieved by loose bowel movements. Twice in the previous two and one-half months she had noted bright red blood with defecation. These attacks had become worse during the past year but were alternated with periods in which she was free from symptoms. She had lost 32 pounds (14.5 Kg.) over the past five years. Roentgenograms of the gastrointestinal tract taken in 1940 had been reported as normal. In 1942 roentgenograms of the colon were first reported as normal, but a narrowing and peculiar configuration of the mucosal pattern seen in the ascending colon led to reexamination. The findings were still indeterminate, as the deformities could

be explained on the basis of accumulated gas and fecal material. Stools contained occult blood. Slight anemia was present. The patient was started on a regimen for functional bowel distress, with temporary improvement. She was seen repeatedly over the next eight months, and when her cramping abdominal pain persisted roentgenograms were again made. On Aug. 13, 1943, fluoros-

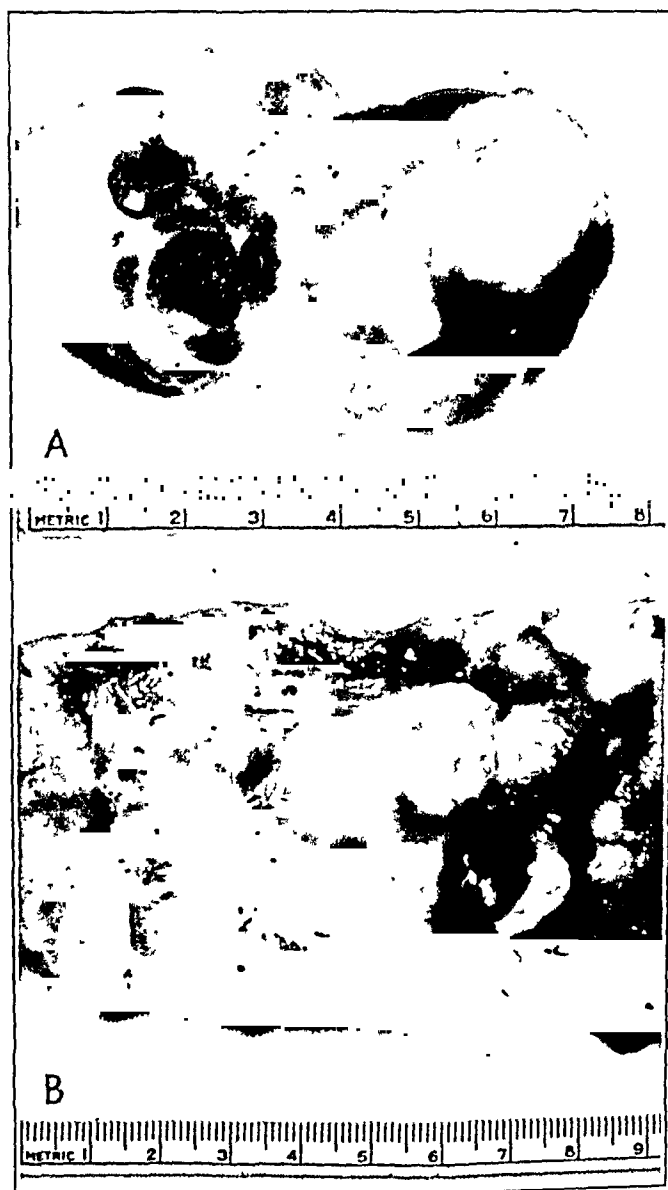


Fig. 5.—*A*, photograph of the lobulated submucous lipoma removed by local excision from the cecum in case 3. *B*, photograph of the resected segment of colon containing the lobulated polypoid submucous lipoma in case 4.

copy revealed a polypoid tumor in the ascending colon causing transitory obstruction.

On August 26 an exploratory laparotomy was performed and a mass palpated in the region of the hepatic flexure which had caused intussusception of the

ascending colon. It was possible to reduce the intussusception, and a 5 to 6 cm. tumor was found apparently attached by a long pedicle to the cecum. The cecum was opened, and the tumor, a lipoma, was removed by cutting the pedicle. The stalk was infolded by two layers of sutures, and the cecum was closed. The resected pedunculated tumor, 6 by 4.5 by 4 cm., weighed 47 Gm. (fig. 5 *A*). There was no ulceration or necrosis grossly, and on cut section the mass appeared to be adipose tissue. The pathologic diagnosis was a nonulcerated submucous lipoma of the colon.

CASE 4.—G. B., a 46 year old man, was first seen on Aug. 18, 1943, complaining of transient attacks of watery blood-tinged stools six to seven times daily for one and one-half years. The associated mild pain in the left flank was relieved by bowel movements. There was increased rumbling and abdominal distention. Roentgenograms of the gastrointestinal tract taken early in the course of his illness were reported as normal, and he was placed on a bland diet with only temporary relief. There was a marked recurrence of symptoms six months before his visit to the clinic.

Abdominal examination failed to reveal any palpable masses but hyperactive peristalsis was noted. Roentgenologic examination revealed a polypoid lesion at the junction of the descending and sigmoid colons interpreted as a carcinoma.

On August 27 a laparotomy was performed and a pedunculated 3 to 4 cm. yellow tumor of the sigmoid colon, believed to be a lipoma, was found. An obstructive Mikulicz type of resection of the segment of bowel containing the tumor was carried out. Three weeks later the colostomy opening was closed.

Examination of the specimen revealed an 8 cm. segment of sigmoid colon containing a polypoid tumor 3.5 by 4 by 3 cm. on the antimesenteric border (fig. 5 *B*). The mucosa was smooth and intact over the tumor. Cut section of the mass showed it to be made of lobulated fat tissue. Microscopic sections confirmed the diagnosis of a nonulcerated submucous lipoma of the colon.

CASE 5.—H. M., a 57 year old man, was seen on Dec. 14, 1945, complaining of cramping pain in the lower abdominal area present for seven months. These attacks of pain, lasting fifteen to sixty minutes, occurred chiefly before meals or at bedtime and were relieved by a bowel movement or by passing flatus. For two or three months he had had diarrhea, and on several occasions he had passed blood. He had lost 15 pounds (6.8 Kg.) of weight during the past six months.

It may be significant that this patient had been seen in 1929 in the Medical Clinic of this hospital with similar complaints. All examinations were non-contributory, and a diagnosis of functional bowel distress had been made.

Physical examination revealed a movable 8 to 10 cm. mass to the right of the umbilicus. Roentgenograms of the colon showed a large mass in the cecum reported to be either a carcinoma or a benign tumor such as a lipoma. The tendency of this lesion to intussuscept into the ascending colon was noted at fluoroscopy.

A laparotomy was performed on Dec. 21, 1945. After dense adhesions in the right lower quadrant were freed, a mass was found in the ascending colon. In the belief that it was a carcinoma, a colectomy, with a side to side ileotransverse colostomy, was performed on the right side.

The specimen consisted of the right colon containing an ulcerated sessile mass 3 by 4 by 3.5 cm. located 2 cm. distal to the ileocecal valve (fig. 6). On cut section the mass was found to be made up of soft cystic fatty tissue. On microscopic examination it proved to be a submucosal lipoma with an ulcerated infected surface (fig. 7).





Fig. 6. —Photograph of the resected portion of the cecum in case 5 showing the polypoid submucous lipoma with an ulcerated surface.



Fig. 7.—Low power photomicrograph of the submucous lipoma with an ulcerated surface removed in case 5.

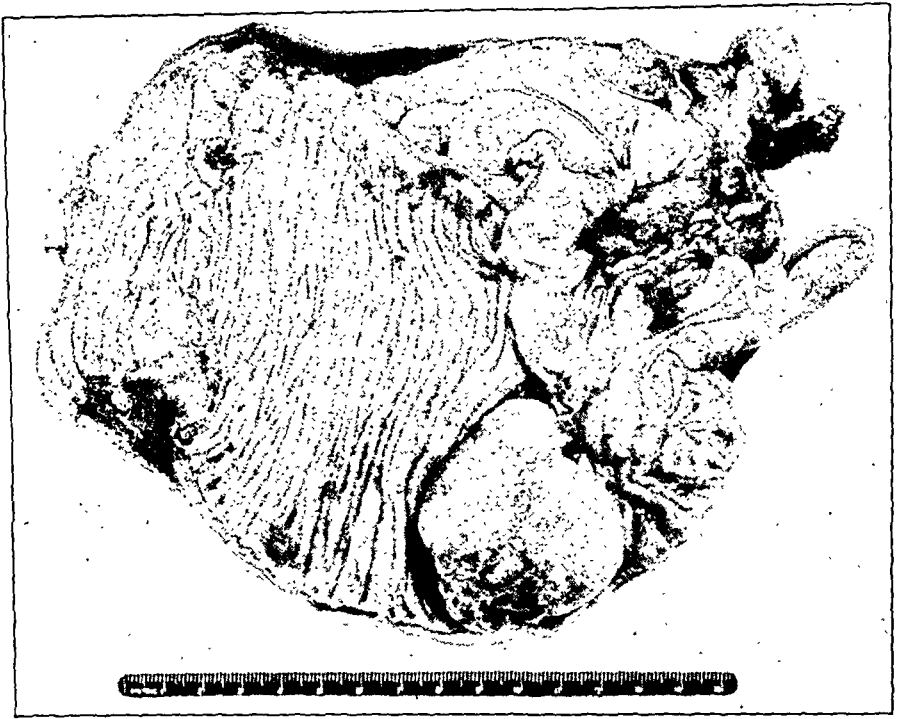


Fig. 8.—Photograph of the resected colon in case 6 showing the submucous lipoma.

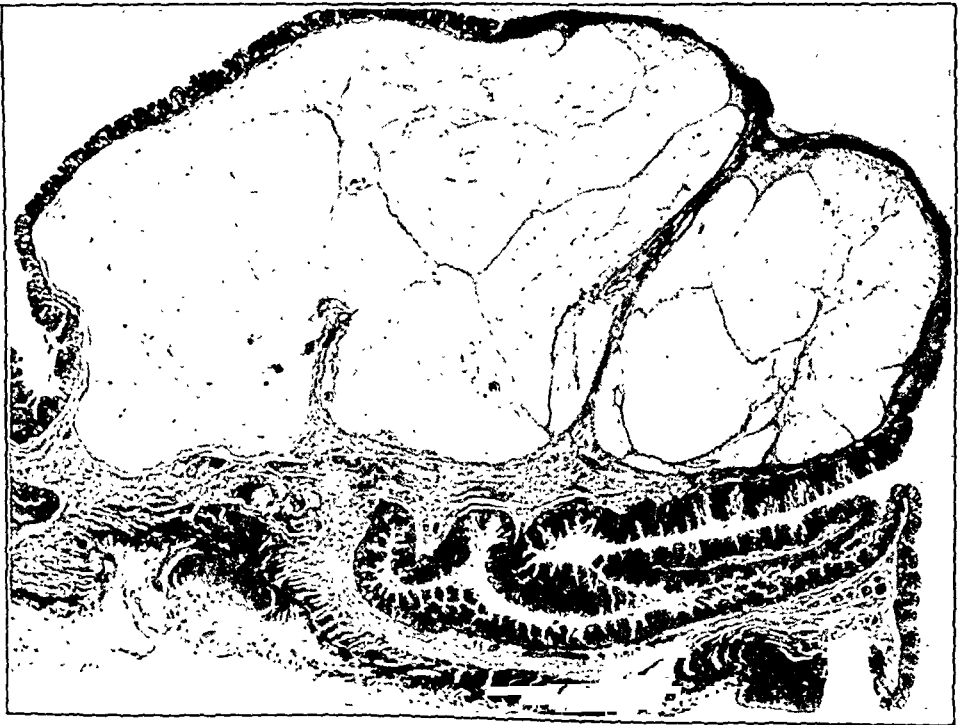


Fig. 9.—A low power photomicrograph of the colon in case 6 containing a submucous lipoma. There is some loss of mucous membrane over part of the tumor.

CASE 6.—J. N., a 57 year old housewife, complained of constipation and sharp stabbing abdominal pain in 1930. A diagnosis of functional colitis was made, and she was treated with a bland diet, with improvement. Roentgenograms of the colon in 1943 were normal.

This patient was next seen in the Surgical Clinic on March 14, 1947, complaining of increasing constipation for six weeks, associated with epigastric cramping pains, anorexia and weakness. One week before entering this hospital a barium enema revealed an intussusception of the ascending colon. This was reduced, and a filling defect in the right side of the colon was demonstrated.

Physical examination revealed a soft flabby abdomen with a large tubular tender smooth mass 10 by 4 cm. on the right side. Roentgenograms of the colon showed intussusception of the terminal portion of the ileum and cecum into the ascending colon. When this was reduced a mass was present in the cecum.

The patient was operated on on March 18, 1947, with a preoperative diagnosis of carcinoma of the cecum. A globular mass was felt in the cecum, and under direct observation the cecum intussuscepted several times into the ascending colon. After palpation it was felt that the lesion was a benign lipoma. Local excision was considered but was decided against because of the sessile nature of the lesion and its close proximity to the ileocecal valve. Colectomy was performed on the right side, a side to side ileotransverse colostomy being used.

Examination of the specimen revealed a 6 cm. polypoid yellow tumor of the cecum covered by intact mucosa (fig. 8). On cut section it was made up of lobulated fat—a typical submucous lipoma of the cecum (fig. 9).

#### COMMENT

Submucous lipomas of the gastrointestinal tract are usually single although Comfort's<sup>16</sup> (13 cases), Humphreys'<sup>18</sup> (4 of 23 cases) and Browne and McHardy's (a recent case) patients had multiple tumors. In 7 cases of this series a single lipoma was present.

Apparently there is no tendency for these tumors to become malignant. They are highly vascular lobulated masses of adult fat cells, located in the submucosa and extending as polypoid or sessile growths into the lumen of the bowel. Their mucosal covering is usually atrophic and flattened from pressure and may be ulcerated. Ulceration was present in 2 of our cases. These tumors vary in size from 1 to 12 cm. in diameter and average about 4 cm. The largest in this series was 6 cm. and the smallest 1.5 cm. in diameter.

Since these lipomas tend to become polypoid, they have a tendency to be pulled out on a long stalk by the peristaltic activity of the intestine. This may result in a dimpling of the serosa at the base of the tumor, a characteristic sometimes seen with other large polypi. This dimpling was not noticed in any of the cases of this series. Large lipomas sometimes show hemorrhage, cystic degeneration, inflammation or necrosis. The only change of this type in this series was the inflammation present in the 2 cases of ulceration.

The order of frequency of the location of these tumors is usually given as cecum, ascending colon, sigmoid colon, transverse colon,

rectum and descending colon, with a preponderance on the right side. In our group one tumor was in the cecum, two were just distal to the ileocecal valve and one each was found at the splenic flexure, in the ascending colon, in the transverse colon and in the sigmoid colon.

In this series the ages varied from 40 to 60, with an average of 53. There were 5 women and 2 men. These figures parallel the age incidence and sex ratio given by Pemberton and McCormack.<sup>21</sup> The duration of symptoms in this group varied from six weeks to six or seven years, with the majority a year or over.

The usual signs and symptoms of submucous lipomas of the colon are not pathognomonic. They are colicky abdominal pain, a palpable tumor, constipation, loss of weight, rectal bleeding and anemia. All our patients with clinically significant symptoms (excluding case 7) reported cramping abdominal pain. Only 3 had a palpable tumor. When a mass is palpated it can be the lipoma itself, fecal material dammed back by the tumor or intussuscepted bowel. Four of our patients reported constipation and 4 at some time had loose stools. Three reported an appreciable loss of weight. Six reported rectal bleeding, but in only 2 cases was it severe enough to cause anemia.

Submucous lipomas may produce three complications—obstruction, intussusception and hemorrhage. All our patients had some degree of obstruction. Intussusception was present in 3 cases, as shown by roentgenograms or during operation. This parallels the 40 to 45 per cent incidence of intussusception reported in the literature. Strangulation with sloughing and spontaneous expulsion of the lipoma through the rectum have been reported in 20 cases. Two of the more recent cases have been reported by Manheim and Peskin<sup>22</sup> and Backenstoe.<sup>23</sup> Rectal bleeding was present in 6 cases. This may be caused by trauma to the tumor caused by fecal material or intestinal motility, by erosion of the mucosa of the tumor, by pressure ulceration of the mucosa opposite the tumor as reported by Saint<sup>4</sup> or by intussusception.

Most writers report two symptom complexes associated with these tumors. One is a chronic course, often years long, of gradually increasing intermittent obstruction. The other is an acute course lasting a few hours or days and terminating in intestinal obstruction which is often precipitated by intussusception. Although intussusception was demonstrated in 3 cases in this group, there were no cases of acute obstruction. The intussusceptions were of the type which recurred and reduced spontaneously.

21. Pemberton, J. De J., and McCormack, C. J.: Submucous Lipomas of the Colon and Rectum, *Am. J. Surg.* **37**:205, 1937.

22. Manheim, S. D., and Peskin, H.: Spontaneous Elimination of a Lipoma from the Sigmoid Flexure, *J. A. M. A.* **118**:1214 (April 4) 1942.

23. Backenstoe, G. S.: Spontaneous Expulsion of Submucous Lipoma of Cecum, *Pennsylvania M. J.* **44**:21 (Oct.) 1940.

# Summary of Case Reports of Colonic Submucosal Lipomas

	1	2	8	4	5	6
Age.....	59	51	10	10	57	57
Sex.....	F	F	F	M	M	F
Duration of symptoms.....	1 yr.	6 wk.	6 to 7 yr.	1½ yr.	7 mo. (possibly 7 yr.)	6 wk. (possibly 13 yr.)
Constipation.....	+	+	0	0	+	+
Diarrhea.....	0	+	+	+	+	0
Melena.....	+	+	+	+	+	+
Cramping abdominal pain.....	+	+	+	+	+	+
Anemia.....	0	+	+	0	0	0
Weight loss, lb.....	0	20 (9.1 Kg.)	32 (14.5 Kg.)	0	15 (6.8 Kg.)	2 (0.9 Kg.)
Palpable mass.....	0	+	0	0	+	+
Roentgen diagnosis.....	Polypoid benign tumor; no obstruction	Polypoid mass (benign or malignant?)	Polypoid tumor	Polypoid lesion, probably malignant but has benign features	Polypoid mass, carcinoma or benign tumor	Organic mass
Location.....	Transverse colon	Splenic flexure	Ascending colon	Junction of descending colon and sigmoid	Ascending colon	Cecum
Intussusception.....	0	0	+	0	+	+
Operation.....	Modified Mikulicz, obstructive resection	Modified Mikulicz, obstructive resection and cholecystectomy	Local excision	Modified Mikulicz, obstructive resection	Colectomy on right side	Colectomy on right side
Size	7.5 × 4.5 × 4.0 cm.	3.5 × 3.5 × 3.5 cm.	6 × 4.5 × 4 cm. (Weight, 17 Gm.)	3.5 × 4.0 × 3.0 cm.	3 × 4 × 3.5 cm.	6 × 6 × 6 cm.

The absence of acute cases probably in part accounted for the absence of mortality in this group of cases. Lazarus and Marks<sup>2</sup> reported a mortality of 11 per cent in the series they reviewed. There were no postoperative complications in the present series.

It is interesting to note that the diagnosis of submucous lipoma of the colon was appreciated at the operating table in 5 of the cases. One was resected in the belief that it was a carcinoma.

With increased experience, the roentgenologists have in many instances been able definitely to make a diagnosis of a benign tumor of the colon in these cases. If the lipoma is of sufficient size, in mucosal relief roentgenograms it often shows up as a radiolucent area. In 2 of our cases the roentgenologist suggested the diagnosis of benign tumor, probably a lipoma. In 3 other cases there were findings suggestive of the possible benign nature of the lesion—movable circumscribed sessile or polypoid tumors in a pliable undeformed bowel. Careful roentgenologic examination of the lesion can, at least in many instances, alert the surgeon to the possibility of the tumor being benign.

Cases 1 and 7 are of considerable interest for the association of the submucous lipomas with carcinoma. In case 1 the patient had undergone a successful resection of a carcinoma of the sigmoid colon seven and one-half years before. She had symptoms of a similar condition on her later admission to the hospital, but exploration showed no recurrence of carcinoma and a submucous lipoma of the transverse colon was resected. In case 7 a preoperative diagnosis of carcinoma of the transverse colon was made, and at operation a carcinoma of the hepatic flexure was found. As an incidental finding a small submucous lipoma was found in the cecum. In the absence of the carcinoma this lipoma could well have passed unnoticed.

Submucous lipomas in our series were treated by three different operations, depending on the diagnosis at the operating table, location and size. One lipoma in the ascending colon was removed at the base of its pedicle. Three lipomas located in the transverse colon, splenic flexure and descending colon were removed by a modified obstructive type of Mikulicz resection. Two tumors in the right side of the colon were removed by means of colectomy.

With improvements in roentgenologic technic and interpretation, the preoperative diagnosis of these tumors becomes a distinct possibility. In a majority of cases evidence suggestive of the benign nature of the lesions can be found during fluoroscopy of the colon. With the possibility of the lesion being a benign lipoma in mind, the surgeon should be able to recognize the lesion at the operating table in a high percentage of cases. The yellow color of the tumors, their pedunculated nature, the dimpling of the serosa at the base of the pedicle, their elasticity on palpation, the absence of infiltration at the base and the absence of

local or distant metastasis will usually allow the surgeon to make the diagnosis. If he is still uncertain, there is no contraindication to opening the bowel for more direct observation of the tumor.

When the diagnosis is made, local resection by enucleation of the tumor or by cutting the pedicle is the operation of choice. There are a few cases in which a local resection of the bowel with end to end anastomosis will be necessary. There is little danger of local recurrence or malignant degeneration of these tumors, so more radical resections are not necessary.

#### SUMMARY

1. Six cases of surgically significant submucous lipoma of the colon and 1 case in which the lipoma was an incidental finding after a resection of the colon for carcinoma are reviewed.

2. A discussion of the frequency, location, symptoms, physical findings, roentgenologic diagnosis and treatment is presented.

3. Recognition of the lesions at the operating table with more consecutive excisions and consequent reduced mortality and morbidity rates is believed to be the desired trend in the management of these lesions.

## PRESERVATION OF THE ANAL SPHINCTER IN SURGICAL PROCEDURES IN THE RECTOSIGMOID REGION

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IN RESECTION of the rectosigmoid region for carcinoma, it has been the practice of a large group of surgeons to remove the anus and the sphincter, substituting a colostomy opening; a smaller, but perhaps no less vocal, group believes that the sphincter can be retained without the penalty of a higher immediate or remote mortality. This amiable feud goes on and on, with concessions from either side, and in all fairness it can be said that both groups have honest convictions. I believe there is enough information available concerning many aspects of the subject to permit some rational decision.

Two questions naturally arise: First, is it possible to retain a functioning anal sphincter without materially increasing the risk of operation and, at the same time, maintain a record of five year cures comparable to that of the colostomizing operation? Second, can the operation be done with the assurance that a normally functioning sphincter will remain?

The abdominoperineal resectionists are responsible for the statement or general impression that only by removing the entire distal end of the gastrointestinal tract can one minimize recurrences of carcinoma. The point is emphasized that by removal of the sphincter and sections of the levator muscles, the path of metastasis is interrupted or obliterated: a colostomy is a necessary by-product. Glover and Waugh<sup>1</sup> have shed much light on the subject of metastasis in carcinoma of the rectum and sigmoid. I believe that no other contribution in recent years has approached the thoroughness of their work, which upsets some generally accepted theories concerning the secondary distribution of cancer in this region.

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1. Glover, R. P., and Waugh, J. M.; The Retrograde Lymphatic Spread of Carcinoma of the Recto-Sigmoid Region, Surg., Gynec. & Obst. 82:434-448 (April) 1946.



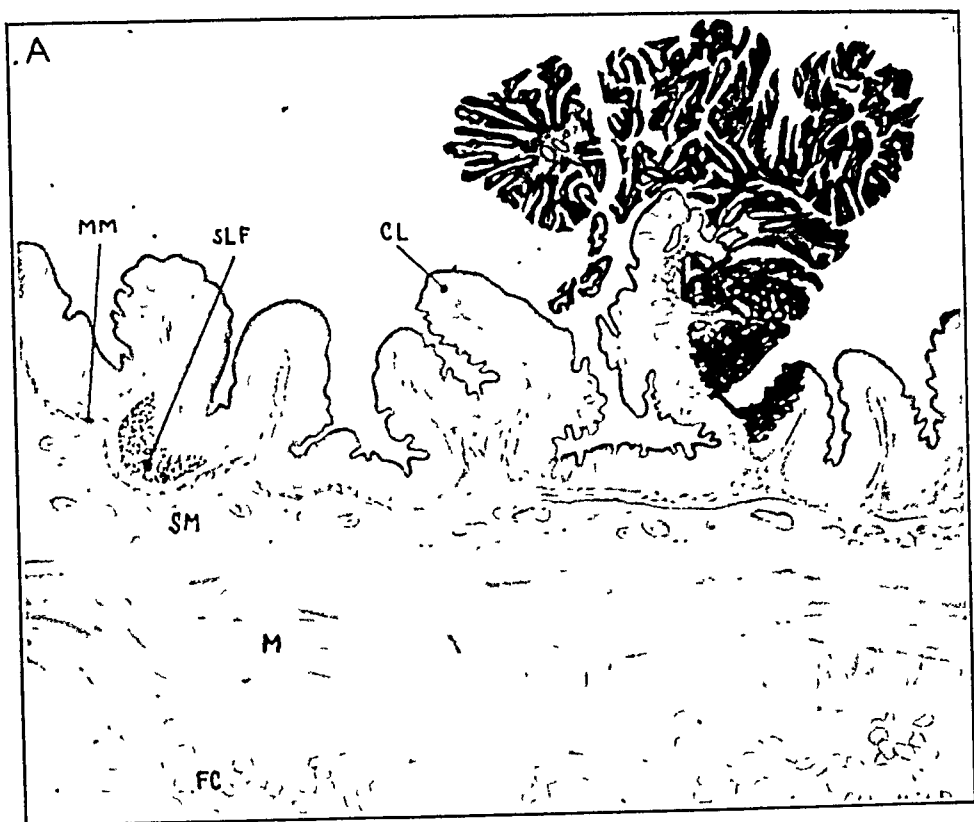


Fig. 1.—Duke's classification of carcinoma of the rectosigmoid: *A*, tumor limited to the wall of the rectum; *B*, spread by continuity to the extrarectal tissues, but not to the regional nodes; *C*, metastasis present in the regional nodes. *MM* indicates muscularis mucosae; *SLF*, single lymph follicle; *CL*, crypt of Lieberkuhn; *SM*, submucosa; *M*, muscle, and *FC*, fat cells

In 100 cases of resection of the rectosigmoid region for carcinoma, Glover and Waugh meticulously went through the operative histories and the pathologic sections. In 20 per cent of the cases carcinoma had spread to the liver by way of the venous channels. In less than 1 per cent were nodes involved more than 2 cm. below the margin of the

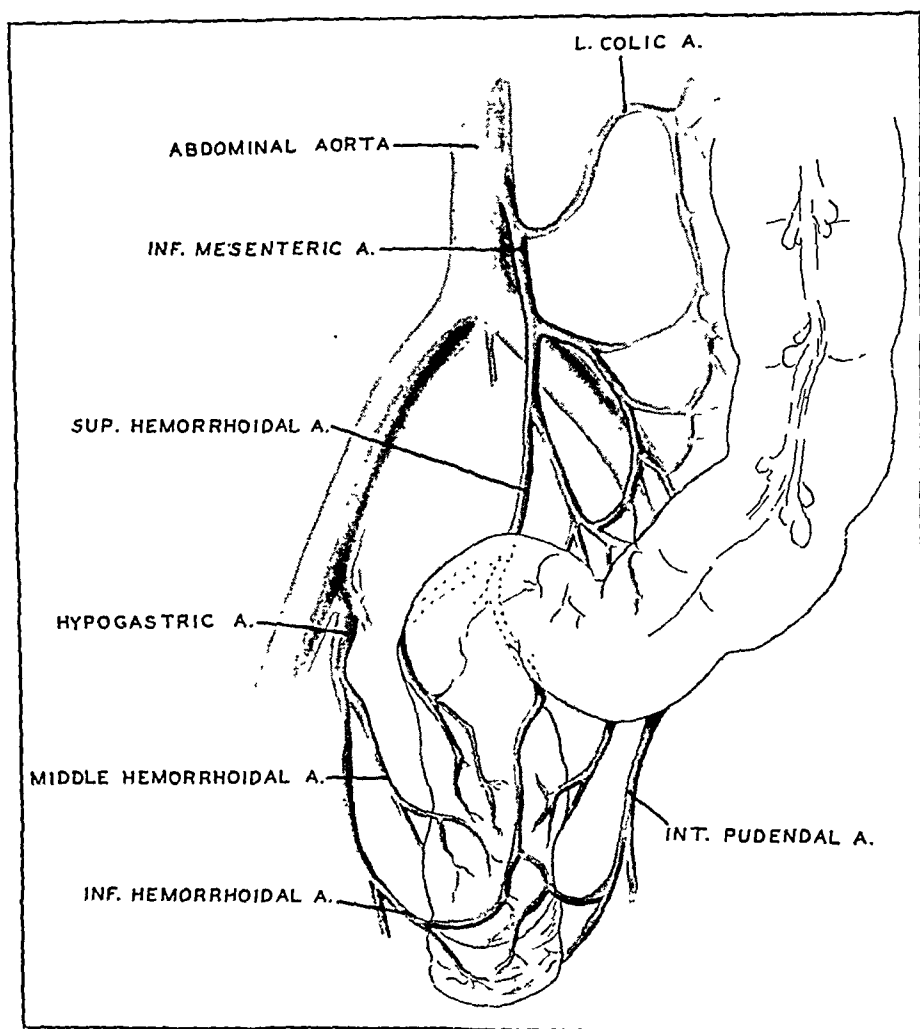


Fig. 2.—Blood supply of the rectosigmoid.

growth. After a careful analysis of the literature, the authors made this statement:

In more than 239 of the 507 cases from the literature in which the removed tissues were completely examined, nodal metastasis was observed to occur. Of these only 8 gave evidence of an involved node below the level of the lesion itself . . . in 7 of the 8 cases there was no spread below the 2 centimeter level,

which when interpreted in the terms outlined in this study remains insignificant. . . . When such retrograde spread can be demonstrated, it is an indication that upward normal channels have been blocked.

It cannot be emphasized too strongly that metastasis via the lymphatics is primarily, if not invariably, upward. The more malignant and extensive the growth, the greater is the chance of nodular involvement. The venous channels should be accorded a high rating in responsibility for secondary lesions, as they furnish avenues for transmission

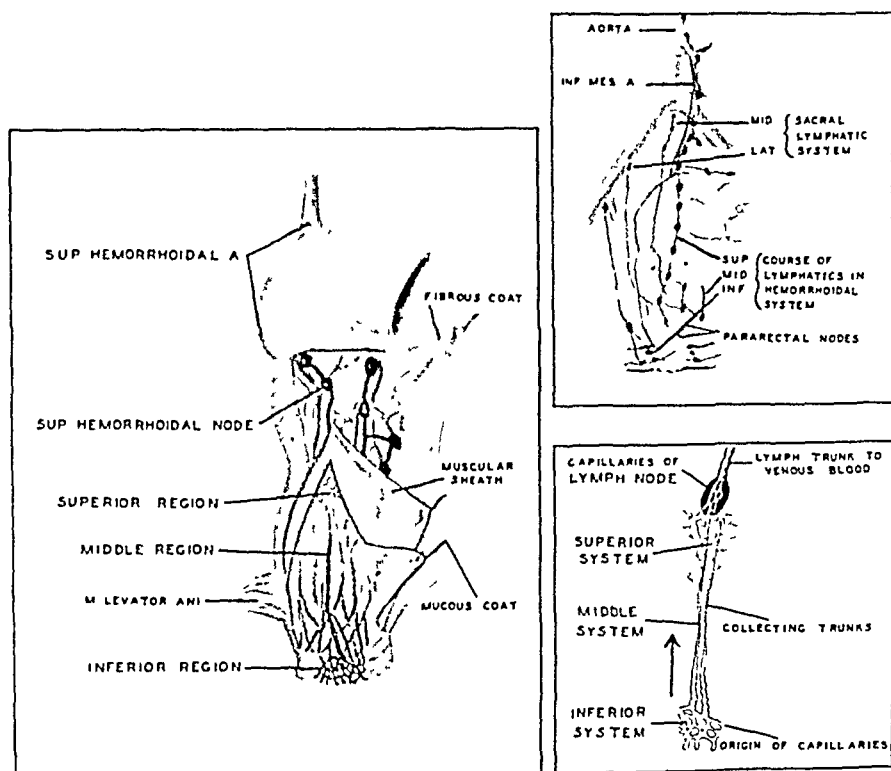


Fig. 3.—Lymphatics of the rectosigmoid.

of the disease; it is not uncommon for one to find extensive hepatic involvement without the lymph nodes having been invaded. It should not pass unnoticed that early recurrence or inoperability is often predicated on an extension to a contiguous structure, and lymphatic involvement may play a minor part in the prognosis. This leads to the conviction, substantiated by the examination of 1,339 nodes by Glover and Waugh, that any growth of the rectosigmoid region resected 2 cm. or more below its lowest palpable margin has a less than 1 per cent chance of metastasis through nodes below this level; it is not necessary

for the anus to be sacrificed if the growth is 6 cm. or more above the pectinate line. Therefore, it would appear that if a resection can be done 2 cm. or more below the growth in this region the sphincter can remain unimpaired and an anastomosis made by one of two methods,

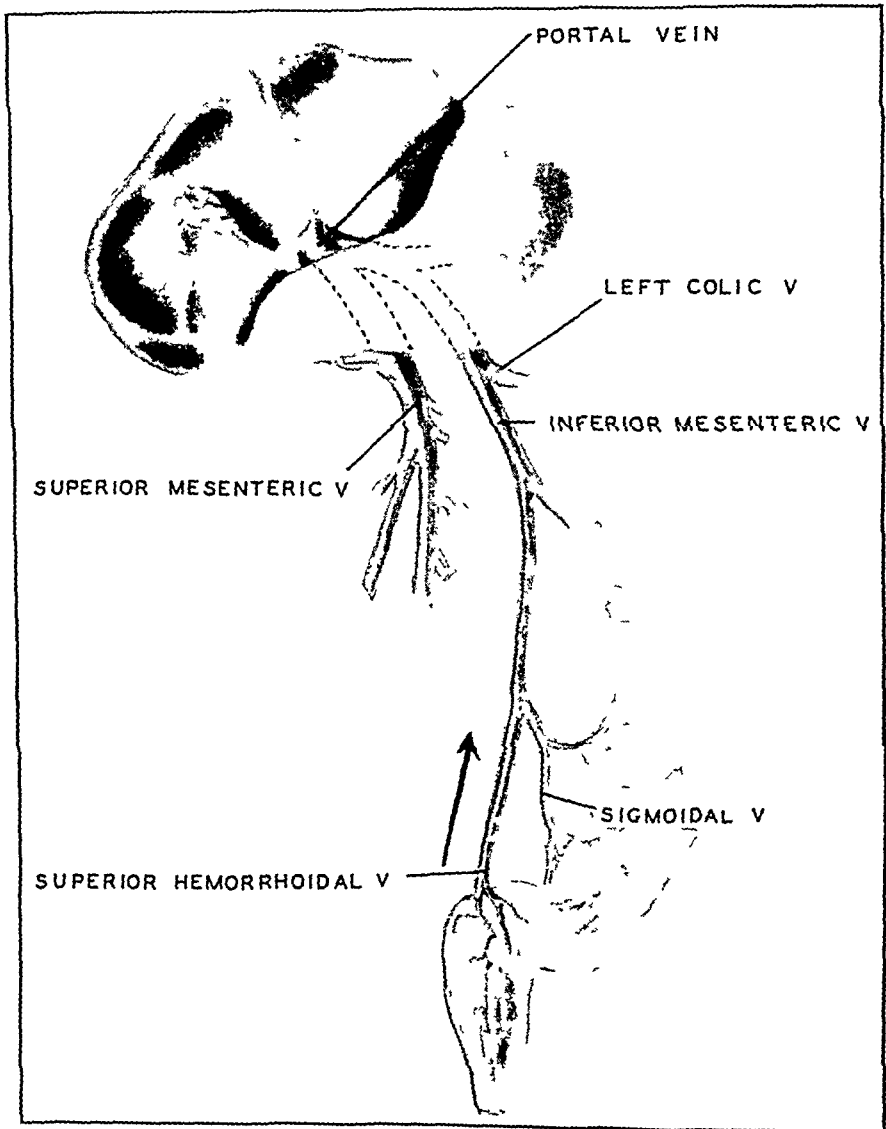


Fig. 4.—Course of hepatic metastasis.

the intra-abdominal method or a combined abdominal and perineal method.

One cannot find fault with the mortality of the combined abdomino-perineal operation in the hands of such excellent operators as Jones or Lahey, but the permanent colostomy opening plagues the operator and

the patient. It is doubtless true that many patients learn to take such excellent care of a colostomy opening that they are never suspected of having an artificial anus, and they pursue gainful occupations. Nevertheless, a colostomy opening is a physical handicap and a mental hazard. I have yet to see the first patient who would not exchange a good colostomy opening for a functioning anus, were it possible for him to make such a transfer. There can be no question that the possibility of a permanent colostomy opening deters many from an operation which could well result in a cure; on the other hand, I never knew of a patient who committed suicide because he was the unproud possessor of a colostomy opening.

Babcock and Bacon have been the chief proponents of the operation to preserve the sphincter, and they are entitled to much credit for their persistent efforts and pioneer work. When this operation has been performed by others, the results have been somewhat disappointing, but the fault may have been with the operator and not the operation. It is impossible for one to predict prior to operation just what sort of sphincter control will follow. Some patients complain of strictures; others of incontinence, with thin stools. All in all, the aforementioned operation seems to fall just short of an ideal procedure. During the past few months I have undertaken to modify the combined abdominal and perineal operation in such a manner that perfect sphincter control is assured. I claim no originality for the operation, as it is merely a revival of a discarded one, discarded because it was cursed with complicating infections.

The introduction of antibiotics in recent years has removed many of the dangers attending intestinal surgery, so that surgeons may, without fear of peritonitis, do an open anastomosis and take other liberties with the gastrointestinal tract never before dreamed of. By the intelligent use of the sulfonamide compounds, penicillin and streptomycin, alone or in selected combinations, and through evacuation and decompression, it is possible for the surgeon to minimize the danger of infections in most intestinal operations. The elimination of infections by these means makes possible the preservation of the anal sphincter in the operation described.

The operation proceeds as in the routine abdominoperineal resection, with a low midline incision from the pubes to the umbilicus, or higher, with the patient in the Trendelenburg position. Exploration for metastasis and estimation of the extent of the growth should be the next steps. The sigmoid is isolated by dividing its peritoneal attach-

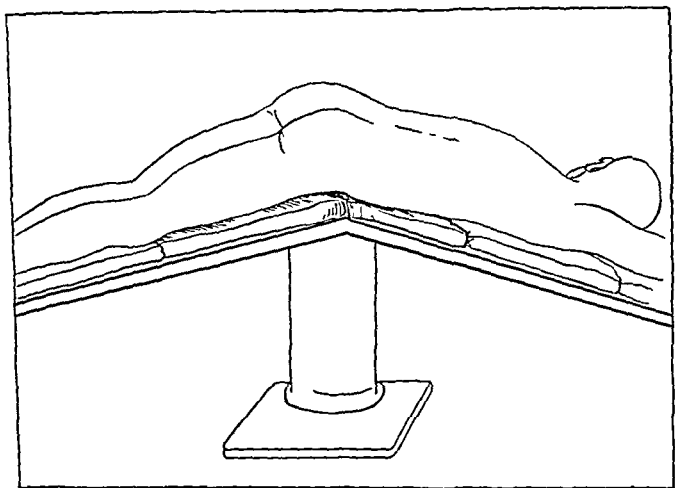


Fig. 5.—Position of the patient at the second stage of the operation.

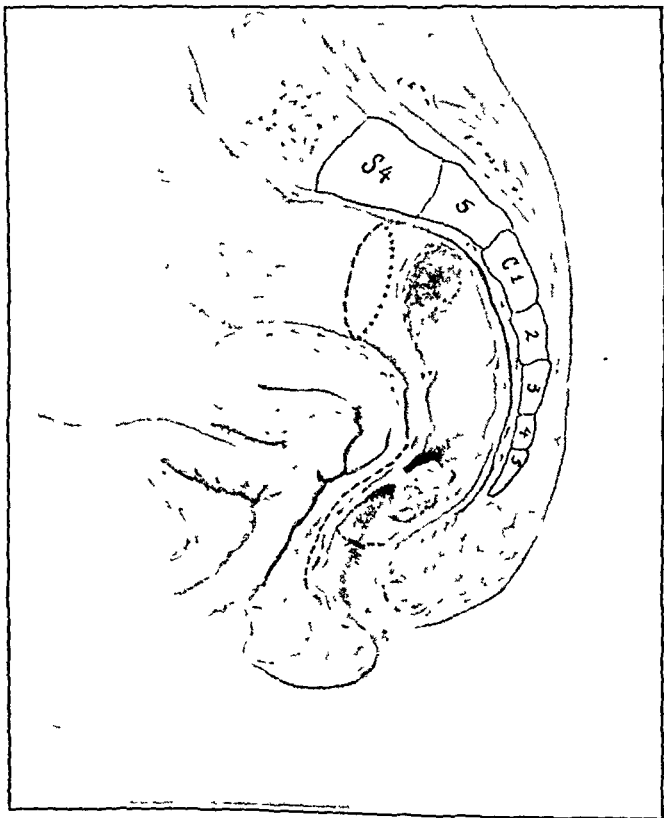


Fig. 6.—Lateral view, carcinoma in situ.

ments laterally and from the bladder, ligating the superior hemorrhoidal vessels and detaching the bowel well down into the pelvis, to the tip of the coccyx. The growth can be palpated and evidence of nodular involvement noted, if present. After the bowel is thoroughly freed, a silk thread may be placed as a marker proximal to the growth, through

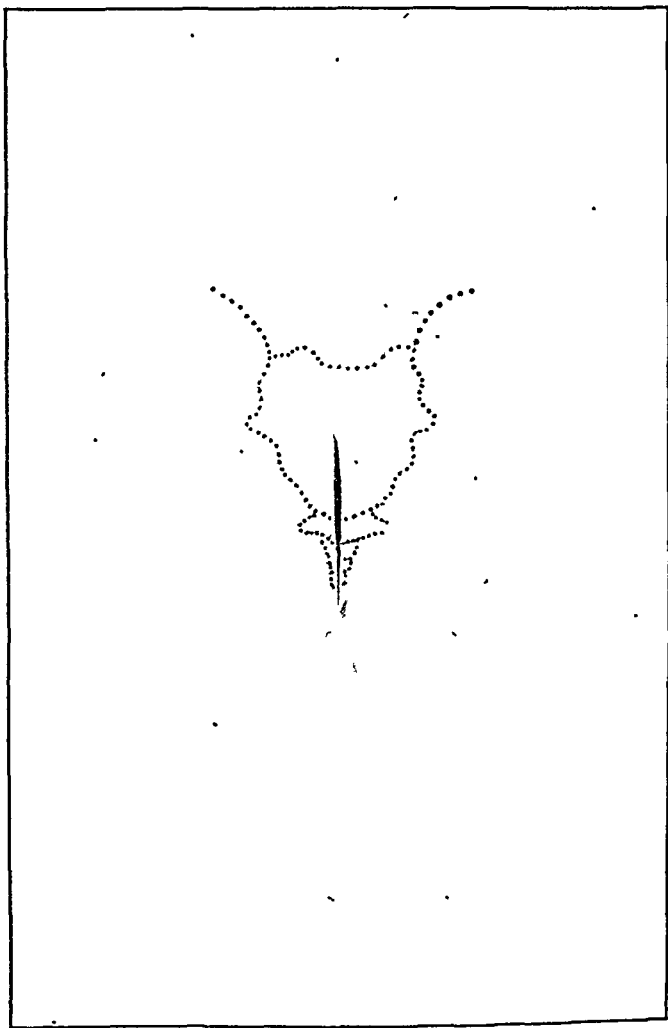


Fig. 7.—Second incision.

the outer coats of the bowel at the lowest point where the circulation in the colon is adequate. The highest level of the sigmoid that can be brought down to the anus depends on the anatomic situation and possibly on the surgeon; Bacon claimed to have brought the transverse colon down in the "pull-through" operation. It is mandatory that the upper end of the resected segment be not lower than its adequate

blood supply. When the segment of the bowel to be resected is completely liberated, all attachments should be divided to permit the segment to be displaced in the pelvis, with sufficient freedom to allow the site of the proposed division of the bowel to be placed in the pelvis without tension. A new floor of the pelvis is constructed from the peritoneum, which has been separated laterally and anteriorly, and closed snugly above the rectosigmoid deep in the pelvis. The abdominal wound is then closed and the patient placed face downward on the

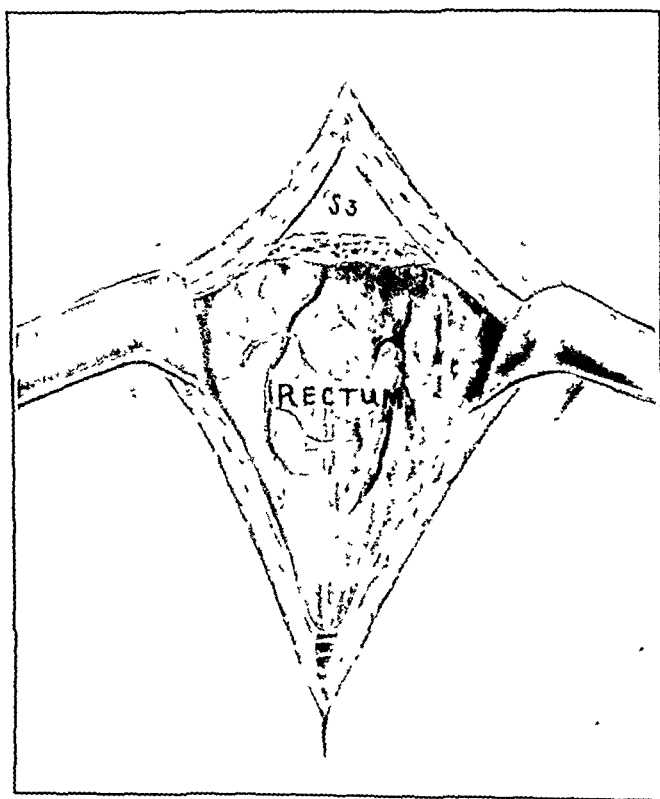


Fig. 8.—Second incision retracted.

table in a jackknife position. The buttocks can be kept apart by adhesive straps for a better approach to the operative field. An incision is made from the middle of the sacrum to 3 cm. above the anus. The wound is deepened and retracted. The coccyx, the fifth and part or all of the fourth sacral segment are removed. The sacral arteries lie near the middle line, close to the pelvic side of the sacrum. They should be ligated and divided. As the separation of the tissues in the midline is continued, the pelvis below the new peritoneal floor is invaded, and the loose rectosigmoid segment can be drawn through



the incision. The marker of silk suture can be identified, and a Stone clamp placed at, or above, this level. About 3 to 4 cm. above the anus a second Stone clamp is applied and the section removed between the two clamps, which are then disengaged. The open ends of the bowel are approximated and held by a guy suture on either side to facilitate the open anastomosis. I use fine chromic surgical gut U. S. P. on atraumatic® needles. The first row is one of the Lembert type and approxi-

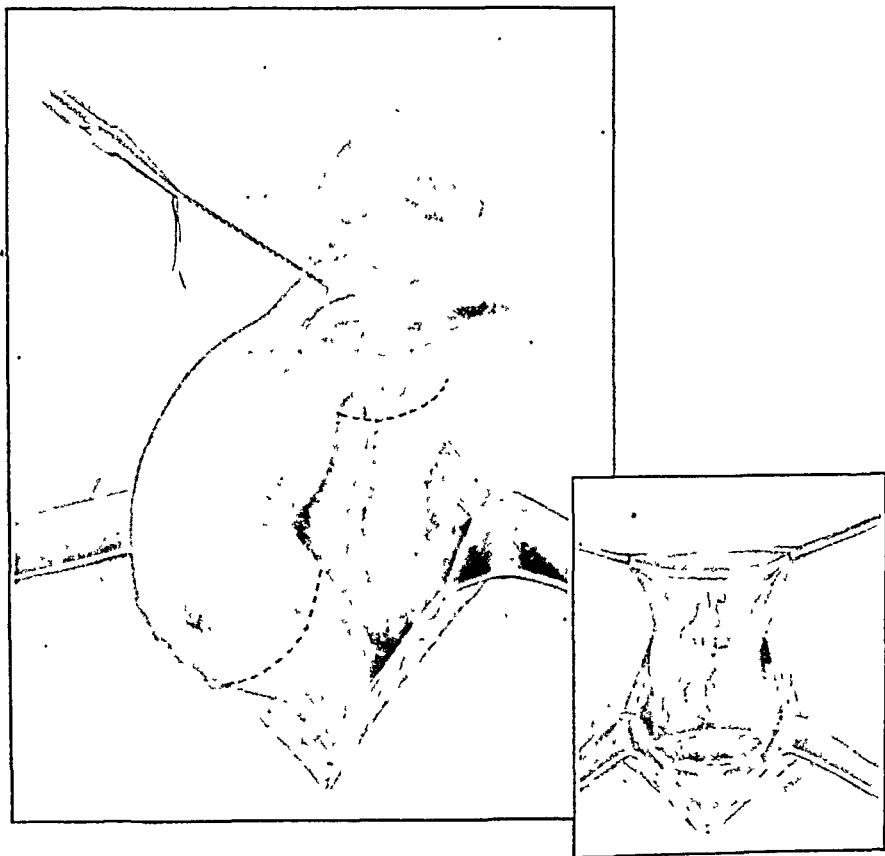


Fig. 9.—Tumor and rectosigmoid segment delivered.

mates the posterior surfaces (anatomically the anterior surfaces); this is followed by a locking stitch through all layers. These two rows of sutures firmly bind the two posterior walls. The binding of the anterior wall is completed by a Connell stitch, over which the last, or Lembert, row completes the anastomosis. The guy sutures are removed, and the bowel is dropped back into the pelvic cavity. A cigaret drain is placed in the lower end of the wound. The use of a rectal tube passed through the anastomosis is optional, as it may prevent edema at the point of

anastomosis. It can be introduced before completion of the anastomosis, to avoid any possible trauma and to insure its proper position in reference to the anastomosis.

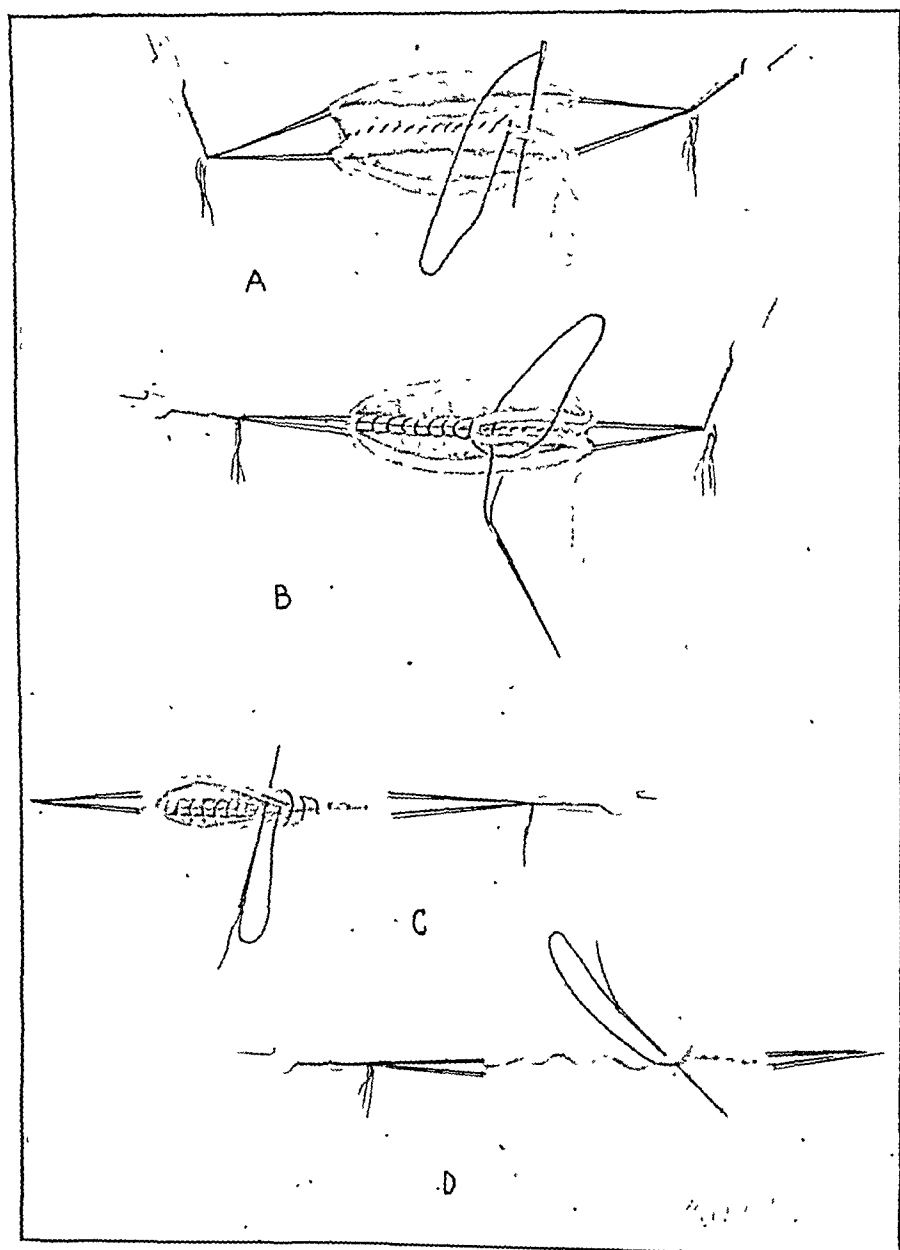


Fig. 10.—Anastomosis, by steps.

The convalescence is a matter of two weeks or less, with excellent sphincter control. My experience with the operation is confined to 10 cases, a number insufficient to permit one to make convincing deduc-

tions, but warranting further exploration in this field. The low end to end intra-abdominal anastomosis in the surgery of the rectosigmoid region, as described and practiced by Dixon, appears to have a wider field of application than that in which it is employed at present. However, so few operators possess the technic and dexterity of Dixon that the operation has not been popularized, notwithstanding its sound

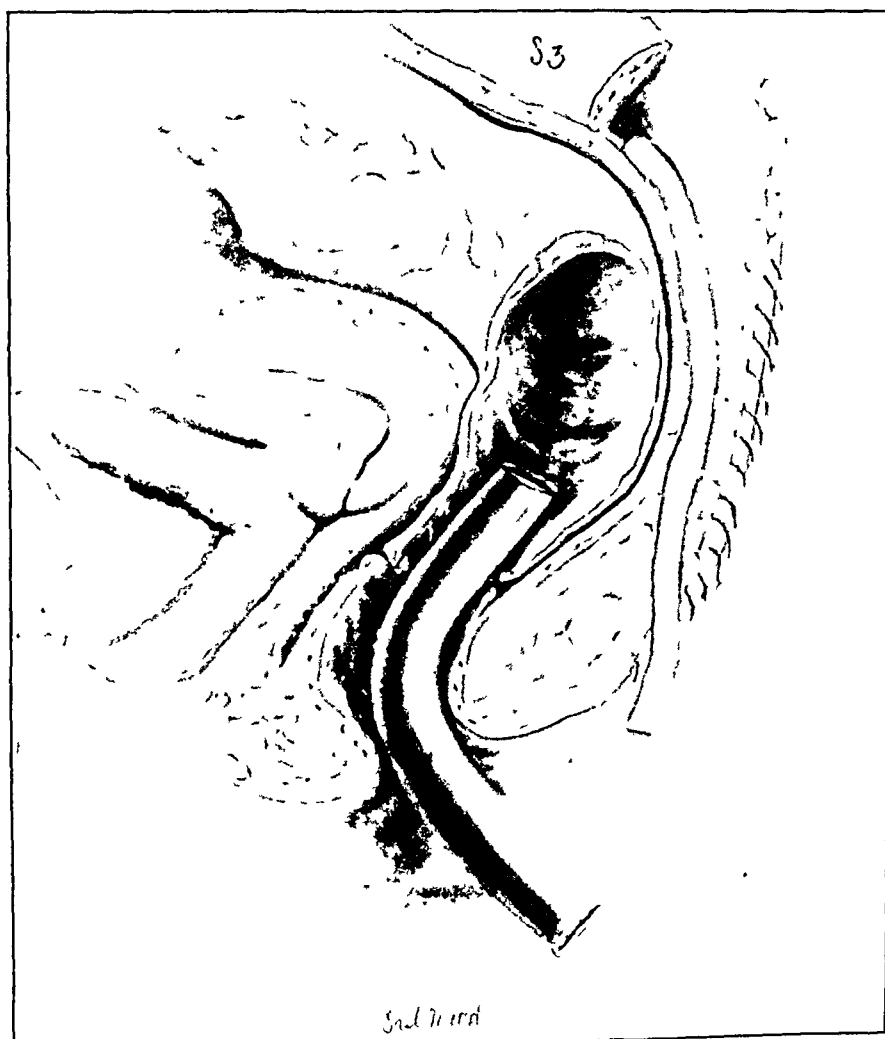


Fig. 11.—Operation completed, lateral view.

principles. To some extent the operation here described is a substitute, particularly in those cases in which the malignant growth is 6 to 15 cm. above the anal sphincter. The operation is illustrated by 4 cases.

#### REPORT OF CASES

**CASE 1.**—M. N., a married white woman, aged 46, a clerk, was admitted to the hospital on Feb. 9, 1947. The chief complaint was bleeding from the rectum.

The patient's mother had died at 75 and her father at 77, both of "bad heart." There was no history of malignant disease in the family. The past medical history revealed the usual childhood diseases without complications. "Thyroid trouble" had been experienced for nine years prior to subtotal thyroidectomy in May 1946; the diagnosis had been Hashimoto's disease (struma lymphomatosa). A hemorrhoidectomy had been done in 1938. In 1922 a bilateral salpingectomy and an appendectomy had been performed. Prior to her present illness the patient had been under observation for two months for a small cystic mass in each breast.

The present illness began eight weeks prior to her admission with the appearance of constipation (for the first time in many years), and the condition had failed to respond to laxatives. Five weeks before her admission dark red blood had been noted in the stools, and this had been present intermittently since. Three weeks prior to admission the patient had begun to have severe, cramping abdominal pain. Some anorexia had been present for the past month. There had been a bowel movement every three or four days during the present illness. Review of the systems showed an essentially normal condition except for moderate dyspnea on exertion.

On examination the patient appeared nervous but fairly well nourished. She was not confined to bed. The normal weight had been 105 pounds (47.6 Kg.), and the present weight was 115 pounds (52.1 Kg.). The pulse rate was 80 per minute; the blood pressure, 120 systolic and 80 diastolic. The head and neck were normal except for a well healed collar incision. The upper outer quadrant of each breast presented a firm, freely movable nodular area, 1 cm. in diameter and nontender. There were no palpable lymph nodes. The heart and lungs were normal. The abdomen was slightly distended. Peristalsis was hyperactive. There were no palpable masses or areas of tenderness. The liver, kidneys and spleen were not palpable. Rectal examination revealed well healed hemorrhoidectomy scars. The sphincteric tone was active and normal. Sigmoidoscopic examination, done prior to admission, revealed a fungating mass on the posterior wall, 10 cm. from the anus; this mass did not involve the circumference of the bowel. Biopsy diagnosis of this mass was reported as adenocarcinoma grade 2.

After routine preparation, a combined abdominosacral resection of the rectosigmoid was done, with primary open, end to end anastomosis just above the internal sphincter. Examination by palpation revealed no evidence of metastasis to the regional lymph nodes or the liver.

Pathologic examination of tissues was reported on as follows: "The specimen submitted for examination consisted of a piece of large bowel measuring 8 cm. in length and 3.5 cm. in diameter. The mucous membrane was seen to be interrupted in various places by small plaques, which were of increased firmness and averaged 4 mm. in diameter. Midway in this piece of bowel was a plaque, measuring 1 cm. in diameter, which was slightly raised and apparently somewhat polypoid. Sections through this nodule revealed it to consist of irregular, anaplastic glands lined with embryonic columnar epithelial cells. The glandular pattern was fairly regular, although the lumens varied greatly in size. The nuclei were hyperchromatic, and mitotic figures were seen in various phases of development. Invasion, however, did not appear to be very deep in the muscular wall. The diagnosis was adenocarcinoma."

The postoperative course was uneventful. The temperature rose to 99.6 F. on the first day and fluctuated between this and normal for five days, returning

to normal. The Levin tube was removed after forty-eight hours, and the patient was given clear liquids freely. The rectal tube was removed on the fifth day. The abdominal sutures and the posterior drains were removed on the sixth day. There was no drainage. Gas was passed freely. There was a normal bowel movement on the tenth day, and the patient was discharged on the twelfth day, with perfect sphincter control. Since the patient's discharge from the hospital her course has been marked by constipation, due to a large neurotic element. On Aug. 15, 1947, digital rectal examination indicated an adequate lumen. Sigmoidoscopic examination revealed complete healing, and the sphincter control has been perfect.

CASE 2.—M. H., a white housewife, aged 35, was admitted to the hospital on Jan. 16, 1947. The chief complaint was vaginal and rectal bleeding. The family history was without significance. The past medical history was essentially non-contributory except for pyelitis for eighteen months, complicated by meningitis (causative organism unknown to me). There was no history of serious illness, accident or operation. The patient had borne three children and was pregnant for the fourth time.

The history of the present illness indicated that in August 1946 the patient had noted bleeding from the rectum. There had been a constant loss of blood in slight amount with occasional spurts of blood. The patient had consulted a physician and had been informed that she had a growth in the rectum. She, however, had determined to have another child before having surgical treatment. The last menstrual period had been in October 1946, and pregnancy was of two and one-half months' duration. After a sigmoidoscopic examination and biopsy of the mass in the rectum, the patient had been advised to have a therapeutic abortion. The specimen taken for biopsy was reported on Jan. 9, 1947 to be of an adenocarcinoma arising in a polyp. On the day prior to admission the patient had begun to have mild vaginal bleeding, and incomplete abortion occurred on the following day. She was taken to the operating room and dilation and curettage was done, with removal of the retained secundines. At this time 2 gold radon seeds, 2 millicurie units each, were inserted into the mass on the posterior rectal wall, 7 cm. from the anus. The patient was discharged from the hospital on January 20, as improved, to be readmitted after a convalescent period of one month.

She was again admitted on February 24, after an uneventful recovery. There had been no loss of weight or gastrointestinal symptoms except for the continuance of slight rectal bleeding. Review of the systems revealed a history of persistent mild headache, relieved by acetylsalicylic acid U.S.P. The patient had hay fever, for which she continually used ephedrine nose drops.

Examination revealed that the patient was well developed and well nourished; the pulse rate was 70 per minute and the blood pressure 128 systolic and 80 diastolic. The head, neck, heart, lungs and extremities were essentially normal. The abdomen was flat, and there was no tenderness, rigidity or palpable mass. The abdominal organs were not abnormal to palpation. Rectal examination revealed normal sphincteric tone. A hard mass could be palpated on the posterior rectal wall. Sigmoidoscopic examination revealed a polypoid, ulcerated mass with elevated edges, bleeding easily, on the posterior rectal wall at a depth of 7 cm.

After intensive preparation over a period of five days, a combined abdomino-sacral resection of the rectosigmoid colon was performed. There was no palpable evidence of metastasis to the liver or the regional lymph nodes. Results of pathologic examination were reported: "Section of the colon disclosed a small cauli-

flower shaped, ulcerated mass, approximately 4 cm. in diameter. The ulceration extended down to the serosa but did not perforate it. Sections revealed numerous irregular glands composed of embryonic epithelial cells, which appeared to be invading in various directions. Their nuclei were hyperchromatic, and mitotic figures were observed. There was an associated moderate fibrosis and dense round cell infiltration. The diagnosis was adenocarcinoma."

The postoperative course was smooth. The gastric suction was discontinued after seventy-two hours. The posterior dressings were changed as necessary because of a moderate amount of serosanguineous drainage. The patient was given clear liquids freely. The rectal tube was removed on the fifth day. On the sixth day the abdominal sutures and posterior drains were removed. The abdominal incision healed by first intention. On the seventh day the posterior sutures were removed. A small sinus with serous drainage persisted for fourteen days, with complete healing. There was a spontaneous bowel movement on the seventh day. The patient was discharged on the sixteenth day, well healed and having bowel movements without aid. Sphincter control was perfect. Since the patient's discharge bowel control has been perfect. The hemoglobin has risen from 65 to 82 per cent. Rectal examination revealed a completely healed, moderately contracted but adequate site of anastomosis through which a proctoscope was passed freely. Examination on Aug. 29, 1947 confirmed this statement.

CASE 3.—B. F., a white woman, aged 55, a housewife, was admitted to the hospital on March 25, 1947. The chief complaint was bleeding from the rectum. The family history was noncontributory. There was no history of malignant disease. The past medical history revealed the usual childhood diseases with no complications. The patient complained of mild arthritis. There had been no serious illness or operation. The menopause had occurred at the age of 50 and had been uneventful. There had been no pregnancies.

The onset of the present illness had been nine months prior to admission, when the patient had noted blood mixed in the stool and at times bright blood prior to a passage. At times the blood had been bright and at times dark. At first the patient had been constipated, but the bowels moved daily at the time of her admission to the hospital. The appetite had been fair, but she complained of some gas and belching. There had been no abdominal pain. Advice had been sought from a physician in another city, who had told her that she had a tumor of the rectum. A specimen for biopsy was taken and reported to be of adenocarcinoma high grade 2. Her weight had been stable at 128 pounds (58.1 Kg.). Review of the systems disclosed an essentially normal condition except for the present illness.

On examination the patient was ambulatory and in a fair state of nutrition, weighing 128 pounds (58.1 Kg.). The pulse rate was 76 per minute, and the blood pressure 140 systolic and 80 diastolic. The head, neck, lungs and heart were not abnormal. The abdomen was flat and free of scars. There was slight infraumbilical tenderness. There were no palpable masses, and the abdominal organs were not enlarged or tender. Sigmoidoscopic examination revealed a polypoid, ulcerated mass on the right posterolateral wall of the rectum, at 12 cm. This mass did not extend around the circumference of the bowel. Anoscopic examination revealed small internal and external hemorrhoids.

After routine preparation of the bowel, a combined abdominosacral resection of the rectosigmoid was done. Primary end to end anastomosis was done 3 cm.

above the internal sphincter. There were no evident metastases to the liver or the regional lymph nodes. The pathologic report was as follows: "Sections through the colon revealed the presence of a malignant process arising in the crypts of Lieberkühn and invading in all directions in a most irregular and haphazard fashion. This invasion included the submucosa and the musculature. The growth maintained an acinous pattern, and the cells were rather embryonic in character, showing the presence of innumerable mitotic figures in all stages of development and having hyperchromatic nuclei. In the deeper structures there were numerous pockets and nests of neoplastic cells. The picture was that of an adenocarcinoma of the 'cylindric cell type of a relatively high grade of malignancy.'"

The postoperative course was uneventful. The Levin tube was removed after forty-eight hours. Flatus was expelled through the rectal tube after seventy-two hours. The rectal tube was removed on the fifth day. On the sixth day a stool was obtained with castor oil. Abdominal sutures were removed on the sixth day, and the incision was healing well. On the seventh day the posterior drains were removed, and the sutures, on the tenth day. The incisions were healing well, and the bowels were functioning adequately with perfect sphincter control on the patient's discharge, on the fourteenth day.

One week after discharge, the patient was seen again. At this time there was a small amount of purulent discharge from the upper end of the posterior incision. The anastomosis was patent and roomy and completely healed. The bowels moved freely, and the sphincter control was perfect. Drainage had stopped, and healing was complete in two weeks. Examination two months later showed that the incisions were well healed, the patient had gained weight and the bowels moved daily. Examination on August 30 showed an adequate lumen and perfect sphincter control.

CASE 4.—H. L., a white man, aged 57, unemployed, was admitted to the hospital on June 14, 1947. The family history was noncontributory, and there was no history of malignant disease. The patient's medical history revealed that in 1924 he had had pulmonary tuberculosis, which had been arrested after one month of bed rest. The disease had become active again in 1937, at which time the patient had been institutionalized for several months. After this treatment he had been under a regimen of complete or partial bed rest for seven years. Again, he had been classified as having an arrested case. In 1915 he had had gonorrhea with stricture of the urethra, responding to dilations only. There had been no operation or serious injury.

The onset of the present illness had been two months prior to admission with constipation, followed by blood-streaked stools for two days. The bleeding had returned one month before and had continued up to admission. There had been no further constipation and no diarrhea. The blood had always appeared bright red. The stools had been of normal size and character. There had been rectal tenesmus for the past month. There had been no loss of weight or digestive disturbance of any kind. The review of the systems showed an essentially normal condition except for the present illness.

On examination the patient appeared well developed and well nourished, with a weight of 157 pounds (71.2 Kg.). The pulse rate was 68 per minute and the blood pressure 130 systolic and 80 diastolic. The head and neck were essentially normal. The chest was clear. The heart was not abnormal. The abdomen showed

no scars, distention, tenderness or rigidity. There were no palpable masses. The abdominal organs were not palpably abnormal. Sigmoidoscopic examination prior to admission revealed a small, villous lesion, raised and bleeding easily, on the right anterior wall at a depth of 13 cm. Biopsy diagnosis was reported as adenocarcinoma grade 1.

Five days prior to admission, the patient was placed under routine preparation for resection of the bowel. Abdominosacral resection was done, with removal of the tumor-bearing area, 10 cm. above and 10 cm. below the lesion. Primary open end to end anastomosis was done 7 cm. above the internal sphincter. There were no evident metastases to the liver or the regional lymph glands. The pathologic report was as follows: "Sections through the colon showed the presence of an extensive malignant process arising from the crypts of Lieberkühn. The pattern in general was glandular. The cells were young. They showed many hyperchromatic nuclei and numerous mitotic figures in various stages of development. There were some ischemic necrosis in the surrounding stroma and a considerable degree of round and plasma cell infiltration. Throughout all coats there were small pockets and nests of neoplastic cells. The diagnosis was adenocarcinoma of the colon grade 3."

The postoperative course was marked by moderate abdominal distention, in spite of Wangensteen suction, and the patient's inability to urinate spontaneously for six days. Gas was passed through the rectal tube on the second day. The Levin tube was removed after seventy-two hours. The colon tube was removed on the fifth day. The abdominal sutures were removed on the sixth day, and the incision was healing well. On the seventh day the posterior drains were removed, and the patient was allowed out of bed. There was a small amount of purulent drainage from the upper end of the posterior incision, and this cleared completely in ten days. On the eleventh day the patient was discharged, with the incision healing well, and with satisfactory bowel movements.

The patient returned to the office at the end of ten days. He was completely healed; bowel movements were satisfactory, and the sphincters were under perfect control. Examination on August 15 showed an adequate lumen with complete healing of the anastomosis.

#### SUMMARY

In cases of malignant growths in the rectosigmoid region, and possibly higher, the anal sphincter may be preserved by a combined abdominoperineal resection, completing the anastomosis through a posterior incision by removing the coccyx and the lower two segments of the sacrum. An open anastomosis is safe if the preoperative preparation takes advantage of the antibiotics now available. Recurrence from metastasis through lymph nodes about the anal stump should be minimal. In less than 1 per cent of cases analyzed has it been shown that lymphatic involvement is present more than 2 cm. below the growth, and then only when higher lymphatics are already invaded. The risk is not increased; sphincter control is complete, and the convalescence is a matter of less than two weeks. The operation requires no greater skill than is employed in routine resections. No originality is claimed for this procedure, as it has been tried and abandoned in the past,



but the inhibition of infection by the antibiotics justifies the revival of the operation. Whether the rate of five year cures will equal that of the abdominoperineal operation with a colostomy is purely speculative at present; but, awaiting statistical data, I believe the operation as I have described it justifies further trial. This operation may prove useful in those cases of ulcerative colitis in which an almost complete colectomy is required. If the terminal few centimeters of the rectum is not involved, an anastomosis with the ileum by the posterior approach may prove practical so that an ileostomy is avoided. I have not had an opportunity to apply this suggestion in actual practice.

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# BLEEDING CONTROL AND ABSORPTION OF SYNTHETIC ADHESIVES

## A Second Report

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IN A PREVIOUS publication<sup>1</sup> the practicability of controlling bleeding in abdominal viscera by the application of synthetic adhesives was demonstrated in rabbits and mice.

Analogues of the commercial so-called Scotch tape were used in enclosing gaps in the liver from which sections had been extirpated. The animals were later killed and the tissue reactions studied. Criteria considered essential for a satisfactory synthetic adhesive were (1) tack, or ability to adhere to viscera or tissue sufficiently to control bleeding; (2) absorbability, with the minimum of surrounding tissue reaction, and (3) sterilization potential.

With the cooperation of the Minnesota Mining and Manufacturing Company, makers of Scotch tape, special synthetic adhesive films have been developed in the attempt to embody these requisites in one tape structure.

As this investigation, begun in September 1943, is concerned with the hemostatic and absorptive qualities of certain particular synthetic adhesives in rats, mice, rabbits, dogs and cats, no attempt has been made at this time for a concurrent comparison with fibrin foam<sup>2</sup> and gelatin sponge.<sup>3</sup>

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Aided by a grant from the Minnesota Mining and Manufacturing Company, St. Paul, Minn.

From the Department of Experimental Medicine, University of Southern California Medical School.

Presented before the Society of Experimental Biology and Medicine, Southern California Chapter, Feb. 23, 1949.

1. Lowry, M. L.: Synthetic Adhesives in the Treatment of Wounds of the Liver and Other Surgical Conditions, *Arch. Surg.* **52**:160-171 (Feb.) 1946.

2. Bailey, O. T., and Ingraham, F. D.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XXI. The Use of Fibrin Foam as a Hemostatic Agent in Neurosurgery; Clinical and Pathological Studies, *J. Clin. Investigation* **23**:591-596, 1944. Bering, E. A., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Fractionation: XX. The Development of Fibrin Foam as a Hemostatic Agent and for Use in Conjunction with Human Thrombin, *J. Clin. Investigation* **23**:586-590, 1944.

*(Footnotes continued on next page)*

## EXPERIMENTAL WORK

These studies are divided into two categories, differing in scope. Section 1 supplements the original preliminary report in search for a nonirritant, absorbable adhesive capable of controlling hemorrhage within the body. Section 2 is concerned with tissue reaction and absorption qualities of the component parts of one specially prepared synthetic adhesive tape.

## SECTION ONE

Rabbits and dogs were used in these experiments. While no effort was made to sterilize the plastic films, an attempt at surgical asepsis was carried on. An operative procedure similar to the original technic was utilized, consisting of the excision in the anesthetized animal of a pie-shaped section of liver  $\frac{3}{4}$  to 1 inch (1.9 to 2.5 cm.) in diameter and the enveloping of the resulting hiatus above, below and at the edge with special adhesive films. No other means of hemostasis was used, and the cut edges of the liver were not brought into apposition. The abdomen was closed with linen sutures and the animal permitted to recover from the ether or pentobarbital sodium anesthetic. Two to seven weeks later the animals were killed and microscopic sections made of the hepatic tissue reaction and the extent of absorption of tape.

*Experiments on Rabbits.*—White male rabbits 4 to 10 months old were used. The anesthetic was ether. Various, specially constructed synthetic plastic films, coated with different synthetic adhesives and forming a clear, transparent tape, were applied at operation.

Abdominal adhesions, while few, were most pronounced in rabbits 1, 4 and 5. In microscopic examinations, sections of liver from rabbits 7, 9 and 10 displayed a minimum scar tissue formation, fading within a short distance to apparently healthy hepatic parenchyma.

*Experiments on Dogs.*—Similar extirpation of sections of liver and enclosure of the wound in a Scotch tape analogue were performed on 7 dogs, all of which made uneventful recovery. Pentobarbital sodium was used intravenously for anesthesia and linen thread for abdominal closure. Autopsy, with microscopic study of the liver, was accomplished on all animals except dog 1, which ran away from his kennel on the fourth week. A specially prepared tape eliminating the rope stock binder, consisting of the polyvinyl alcohol film faced with synthetic resin, was the adhesive tape used in all these animals.

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3. Jenkins, H. P., and Janda, R.: Studies on the Use of Gelatin Sponge or Foam As an Hemostatic Agent in Experimental Liver Resections and Injuries to Large Veins, *Ann. Surg.* **124**:952-961, 1946. Jenkins, H. P.; Sena, E. H.; Owen, H. W., and Jampolis, R. W.: Present Status of Gelatin Sponge for the Control of Hemorrhage, *J. A. M. A.* **132**:614-619, 1946.

In none of the animals was any gross hepatic damage evidenced; microscopic examination revealed normal hepatic parenchyma a short distance from the extirpation wound. The hepatic reaction was a mild scar, not an abscess, and intra-abdominal adhesions were at a minimum, except in dog 3, which had a draining sinus.

TABLE 1.—*Experiments on Rabbits*

Rabbit	Tape	Results
1	Polyvinyl alcohol, Buna S	Uneventful recovery; killed 14 days postoperatively; intrahepatic cyst; mild fibrous capsule; particles of undissolved tape
2	Polyvinyl alcohol, Buna S	Died 6 hours postoperatively, from liver hemorrhage
3	Polyvinyl alcohol, Buna S	Uneventful recovery; killed seventh postoperative day; intrahepatic cyst; mild fibrous capsule; undissolved tape
4	Polyvinyl alcohol, rope stock filler, synthetic resin	Uneventful recovery; killed at 14 days; intrahepatic abscess; heavy fibrous capsule reaction; undissolved tape
5	Polyvinyl alcohol, rope stock, synthetic resin	Died on third day of diffuse peritonitis
6	Polyvinyl alcohol, synthetic resin (without rope stock filler)	Uneventful recovery; killed at 7 days; small intrahepatic cyst; mild fibrous reaction; undissolved tape
7	Polyvinyl alcohol, synthetic resin (without rope stock filler)	Uneventful recovery; killed at 14 days; small intrahepatic cyst; mild fibrous capsule; undissolved tape
8	Polyvinyl alcohol, synthetic resin	Uneventful recovery; killed at 14 days; intrahepatic cyst; mild fibrous capsule; undissolved tape
9	Polyvinyl alcohol, synthetic resin	Uneventful recovery; killed at 21 days; small intrahepatic capsule with particles of undissolved tape
10	Polyvinyl alcohol, synthetic resin	Uneventful recovery; killed at 28 days; small intrahepatic capsule; mild fibrous tissue reaction; particles of undissolved tape

TABLE 2.—*Experiments on Dogs*

Dog	Results
1	Ran away at four weeks, before reoperation; apparent complete recovery
2	Killed four weeks postoperatively; small hepatic scar, within which were particles of undissolved tape; no intra-abdominal tape discovered
3	Killed at three weeks; small hepatic scar; draining sinus from omentum in region of operative wound; while no tape was found, it is a possible cause of the draining sinus, although a previous gastroenterostomy should be considered
4	Killed at five weeks; small intrahepatic cyst; tape found absorbed in abdomen, with practically no surrounding reaction
5	Killed at six weeks; small intrahepatic scar; tape not found within liver or abdomen
6	Killed at seven weeks; mild hepatic scar; tape not discovered in liver or abdomen

*In Vitro Absorption.*—Small squares of tape of (1) cellophane, rope stock, crude rubber; (2) acetate fiber, rope stock, polyisobutylene; (3) polyvinyl alcohol, rope stock, synthetic resin; (4) polyvinyl alcohol, Buna S (without rope stock), and (5) polyvinyl alcohol, synthetic resin (without rope stock) were immersed in (a) tubes of gastric juice aspirated from a healthy male (free hydrochloric acid, 35 degrees; total acidity, 50 degrees) and (b) tubes of normal blood serum.

At the end of four weeks none of the synthetic tape structures was dissolved in the gastric juice nor in the human blood serum.

## SECTION TWO

As a result of the first phase of these investigations, the tape found to incorporate the most promising properties of (1) bleeding control and (2) absorbability, with minimum tissue reaction, was the synthetic resin adhesive coated directly on a polyvinyl alcohol film. An intensive study of these two complex chemical substances, both individually and as a combined adhesive tape unit, was undertaken in rabbits, rats, mice and a cat.

To insure an absorption study of the material definitely within the liver and the spleen, the technic of placing the film over a pie-shaped excision was abandoned. Instead, these vascular organs were incised transversely, in the manner of a sandwich slice. The material to be studied was placed deep in the crevice between the two layers, which were then approximated without the use of a needle suture. The upper and lower portions were held together in most cases by sticking the synthetic resin-polyvinyl alcohol tape around the wound. In a number of instances a special liquid synthetic adhesive, similar in chemical composition to the inserted material, was introduced within the liver or spleen to keep the layers in apposition. It was always possible to control the viscus bleeding sufficiently to allow adherence of the plastic tape; digital pressure with gauze aided in temporarily drying the bleeding bed sufficiently to permit sticking of the adhesive film. An annoying technical problem is the tendency of the sticky film to adhere to gauze and scissors, a difficulty which can be overcome by wetting the cutting instrument.

Another method for implantation of the synthetic resin, the polyvinyl alcohol film and the combined plastic film was the slitpocket wedge incision on the surface of the liver or spleen, with the material held in place by an envelope of adhesive film over the viscus groove. In a few spleens the film was drawn completely through a sagittal incision.

Ether was the anesthetic, and linen thread was used for the closure of the abdomen. The animals, returned to their cages and given a normal diet, were killed at intervals of from one week to eight months later, the abdominal cavity observed for tissue reaction and microscopic sections of the liver and spleen examined for absorption data on the implanted materials.

Three synthetic materials were studied in 235 animals. When the synthetic resins were used (table 3), the weights of the implanted globules of this rubbery mass varied from 25 to 350 mg. The portions of transparent polyvinyl alcohol film (table 4), when inserted, weighed from 7 to 80 mg., with the squares ranging from 2 to 6 cm. in width.

Similar but slightly heavier particles were implanted in the complete tape study (synthetic resin adhesive on a polyvinyl alcohol film, table 5).

Experiments on intraperitoneal absorption were accomplished by implanting particles of similar materials within the abdominal cavity,

TABLE 3.—*Synthetic Resin Implant*

A. Liver									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	3	1	2	4	1	..	..	12
Not found.....	..	..	1	1	1	..	..	..	3
B. Spleen									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	1	1	1	..	..	..	..	4
Not found.....	..	..	..	1	1	..	..	..	2
C. Intrascapular									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	3	3	5	11	3	..	..	..	25
Not found.....	..	1	1	2	1	..	..	..	5
D. Intra-Abdominal									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	2	2	3	9	6	2	..	..	24
Not found.....	..	1	2	1	2	1	1	..	8

TABLE 4.—*Polyvinyl Alcohol Film Implant*

A. Liver									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	2	1	1	3	1	..	..	9
Not found.....	..	1	1	2	2	..	1	..	7
B. Spleen									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	1	..	..	1	1	1	..	5
Not found.....	..	..	..	1	1	..	..	..	2
C. Intrascapular									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	2	1	3	8	4	..	..	19
Not found.....	..	1	..	1	1	1	..	..	4
D. Intra-Abdominal									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	2	1	..	4	4	3	1	..	15
Not found.....	..	..	1	3	4	8	4	..	20

closing the incision with linen sutures and subjecting the animals to autopsy later at various intervals.

Subcutaneous absorption was studied by a technic devised by Lattes and Frantz,<sup>4</sup> in which the material is inserted into a tunnel under the skin of the back through a small transverse intrascapular incision.

For convenience in tabulation, the rabbit, mice and rat experiments are grouped under one heading. Both the rabbit and the mouse were early discarded as experimental animals, the former because of susceptibility to infection and the latter on account of technical operative difficulties with the tiny livers and spleens. Surgical asepsis is not

TABLE 5.—*Polyvinyl Alcohol-Synthetic Resin Tape Implant*

A. Liver									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	1	1	2	2	..	1	..	8
Not found.....	..	..	..	..	3	2	..	1	6
B. Spleen									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	1	1	1	..	..	..	1	5
Not found.....	..	1	..	1	1	..	..	..	3
C. Intrascapular									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	1	1	1	1	1	..	..	..	5
Not found.....	..	..	1	..	1	..	..	..	2
D. Intra-Abdominal									
Months									Total
	1	2	3	4	5	6	7	8	
Found.....	7	3	3	4	5	5	1	..	28
Not found.....	..	3	3	2	3	2	..	1	14

TABLE 6.—*Percentage of Autopsies in Which Material Was Not Found*

	Synthetic Resin	Polyvinyl Alcohol Film	Polyvinyl Alcohol-Synthetic Resin Tape
In liver.....	20	44	43
In spleen.....	33	28	37
Intrascapular.....	17	17	28
In abdomen.....	25	57	33

mandatory in surgical procedures on the hardy rat, a rodent with a large liver and spleen. Of the animal experiments, 90 per cent were accomplished on rats. Application of tincture of iodine and shaving of the abdominal hair was the only operative preparation. In no case was the inserted material itself sterilized.

Though the results in the spleen and intrascapular region were similar, in the liver and abdomen the polyvinyl alcohol film disappeared twice as often as the synthetic resins.

4. Lattes, R., and Frantz, V. K.: Absorbable Sponge Tests, *Ann. Surg.* 121: 894-896, 1945.

## CLOSURE OF TRACHEOTOMY WOUND

A tracheotomy wound in a cat was covered by sticking a small section of the polyvinyl alcohol-synthetic resin tape around the tracheal opening and suturing the skin above. The animal made an uneventful recovery, with a return of normal breathing, and was killed fourteen weeks later. The tracheotomy wound had closed over completely, and no trace of the synthetic adhesive tape was discovered. Microscopic sections showed cartilage regeneration.

## CONTROL EXPERIMENTS

Five rats and 5 mice had large sections of their livers removed, with no synthetic adhesive tape covering and no attempt made to stop the bleeding in the liver. Six of the animals succumbed within one hour after abdominal closure and 2 within four hours, another died ten hours later and 1 animal recovered.

## STERILIZATION EXPERIMENTS

Autoclaving the polyvinyl alcohol-synthetic resin tape for twenty minutes at 120 degrees C. and 20 pounds (9.1 Kg.) pressure resulted in a change in form of the film structure, a sort of melting-down process. The adhesiveness and elasticity were only mildly altered. It might presumably be possible, with suitable equipment, to retain these essential properties of the tape under steam sterilization.

Experiments on sterilization by irradiation from the ultraviolet lamp, while not conclusive, offered promise.<sup>5</sup> Pieces of polyvinyl alcohol-synthetic resin tape were contaminated with pathogenic microorganisms (*Staphylococcus albus* and *Bacillus subtilis*) placed in Petri dishes in suitable culture mediums and exposed to rays from a special ultraviolet filament at varying distances and lengths of time. Although incubated cultures at twenty-four and forty-eight hours were not sterile, there was a marked inhibition of pathogenic growth in the plates exposed to ultraviolet rays as compared to those not exposed to irradiation. It is possible that the plastic tape, while transparent, may interfere with the transmission of the particular ultraviolet rays—a not insurmountable sterilization problem.

## COMMENT

Although the preliminary report demonstrated the feasibility of checking hemorrhage in abdominal viscera of animals with synthetic adhesives, none of the tapes used was sufficiently nonirritating to warrant final consideration. It was recognized that cellophane and the rope

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5. The sterilamp, supplied by the Westinghouse Electric Company, was used.



stock filler both were the cause of considerable tissue reaction. Neither crude rubber, polyisobutylene nor Buna S appeared satisfactory as an adhesive in bleeding control.

The development, through the cooperation of the Minnesota Mining and Manufacturing Company, makers of Scotch tape, of a synthetic adhesive coated directly onto a polyvinyl alcohol film without an intervening rope stock paper binder is a notable advance in the search for an innocuous adhesive capable of controlling bleeding and of being absorbed.

This thin, transparent substance produced remarkably little visceral tissue reaction in the 10 rabbits and 7 dogs of the first section of the present study. In many instances the material, while apparently halting the bleeding in the liver, was itself not found on autopsy weeks later.

The possibilities of overlooking this transparent material, when still unabsorbed in the abdomen, being realized, a technic was developed for implanting the tape directly inside a pocket incision of the liver and spleen. These organs were selected as representing maximum difficulties in hemostasis. It was also essential to examine separately the tissue reactions of the component parts of this tape structure.

Polyvinyl alcohol ( $\text{CH}_2\text{CHOH}$ )<sub>x</sub> is a synthetic product manufactured by the hydrolysis of polyvinyl acetate. It is a ketose between starch and sugar, a white, tasteless and odorless powder dissolving in water, depending on the degree of polymerization. As much as 63 Gm. of polyvinyl alcohol was given daily to dogs by intravenous infusion for twenty-three days by Hueper, Landsberg and Eskbridge,<sup>6</sup> with no appreciable changes at autopsy other than an accumulation of the colloid material in the reticuloendothelial cells of the spleen, liver, kidney and lymph nodes and the formation of atheroma in the large vessels. As in cholesterol atheromatosis, these changes occur only after highly excessive and continuous intravenous administration of polyvinyl alcohol. Hueper<sup>7</sup> found polyvinyl alcohol a relatively inert substance, exerting a definite effect on the coagulation process. In the test tube, with the polyvinyl alcohol blood content more than 3 per cent, an anticoagulant action was produced, caused possibly by mechanical obstruction of the fibrinous network. Hueper also injected as much as 2,700 cc. of a 5 per cent polyvinyl alcohol solution in isotonic sodium chloride solution intraperitoneally, with no more untoward reaction than a temporary hydremia, such as is often observed after acacia injections.

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6. Hueper, W. C.; Landsberg, J. W., and Eskbridge, L. C.: Effects of Polyvinyl Alcohol on Blood, *J. Pharmacol. & Exper. Therap.* **70**:201-215, 1940.

7. Hueper, W. C.: Polyvinyl Alcohol Atheromatosis in Dog Arteries, *Arch. Path.* **31**:11-25 (Jan.) 1941.

The synthetic resin adhesive of this tape structure is an acrylic ester. MacKenzie, Sharpless and Millard,<sup>8</sup> Edds<sup>9</sup> and Brown,<sup>10</sup> among others, have demonstrated the minimum tissue reaction to implants of methyl methacrylate in facial and dental reconstructive surgery. Photomicrographs taken three months after these implants showed a surrounding fibrous sheath with no acute inflammatory or necrotic processes. The synthetic resin, acrylic esters—a gummy, extremely adherent material rolled into a ball-like mass—used in the present experiments, was removed directly from the sticky face of the specially constructed polyvinyl alcohol—synthetic resin tape.

According to table 6, the percentage of animals in which synthetic resin implants were found in the liver and spleen is double that in which polyvinyl alcohol was found. The lack of tissue reaction also favors polyvinyl alcohol over the acrylic esters. Apparently, cyst formation often accompanies implantation of the synthetic resins in the liver and spleen, although the immediately surrounding parenchyma is usually normal. It is possible that these small cysts result from the thick consistency of the implanted ball of synthetic resins—in contrast to the thin film of polyvinyl alcohol. The most pronounced tissue reaction with polyvinyl alcohol occurs when the film curls up into a roll—a tendency of this material. Naturally, the smaller implants cause less reaction, while secondary infection greatly increases the amount of scar.

In the intrascapular implants both the polyvinyl alcohol and the synthetic resins were usually found lying inert in the subcutaneous tissue, surrounded by a thin fibrous capsule and completely devoid of any inflammatory or necrotic process. More rarely a fibrous capsule may encase the polyvinyl alcohol film or the synthetic resin implanted within the peritoneal cavity; abdominal adhesions are not usual. Animals in which the implanted material was not located after careful search at autopsy were still classified under the heading of "not found" rather than "dissolved" because of the possibility of overlooking the thin, transparent film, although it was obvious in the microscopic sections of the livers and spleens that definite autolysis was taking place in the implanted foreign body. Apparently, according to table 6, some enzyme within the peritoneal cavity acts to cause a greater percentage of synthetic adhesive dissolution than with the subcutaneous implants. In the case of the polyvinyl alcohol film, that placed in the liver disappeared more often than that implanted in the spleen. For all three materials—the combined polyvinyl alcohol—synthetic resin tape,

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8. MacKenzie, C. M.; Sharpless, D. H., and Millard, P.: Tissue Reactions to Vitallium and Acrylic Implants, *Northwest Med.* **44**:277-282, 1945.

9. Edds, M. V., Jr.: Prevention of Nerve Regeneration and Neuroma Formation by Caps of Synthetic Resin, *J. Neurosurg.* **2**:507-513, 1945.

10. Brown, A. M.: Methyl Methacrylate Useful in Facial Corrective Surgery, *Arch. Otolaryn.* **39**:179-182 (Feb.) 1944.

the synthetic resins alone and the polyvinyl alcohol film—the lowest incidence of disappearance was found with the intrascapular (subcutaneous) procedure.

The question arises, if dissolution of these synthetic adhesives is possible within the body, why has not a greater percentage of these materials disappeared within the experimental animals? At the present time a precise answer cannot be given, although the size, amount and compactness of the implanted material appear as important factors in the possible process of autolysis. Infection also predisposes to non-absorption, a heavier connective tissue reaction often enclosing a caseous, infected mass. This untoward reaction, in spite of the non-sterilization of the synthetic adhesives, was local and infrequent and abetted by a curling up of the material into a thick lump.

Also, in the manufacture of the polyvinyl alcohol film, small amounts of other chemicals are added as plasticizers to impart certain physical qualities to the synthetic tape. These and other process factors undoubtedly alter tissue insert characteristics. Additional studies to clarify further problems of absorption and bleeding control are now in progress and will be incorporated in a third report, soon to be released.

It is not the intention of the present investigation to offer polyvinyl alcohol or the acrylic esters, in their present stage of development, as suitable for use in the control of bleeding in man. These studies have not as yet reached the clinical trial stage, but the definite absence of parenchymal damage, the paucity of connective tissue stimulation and the complete lack of generalized toxic reactions make it probable that some forms of the synthetic adhesives polyvinyl alcohol and acrylic esters may eventually be incorporated into a plastic tape capable of controlling bleeding within the human body. Of the two substances investigated, polyvinyl alcohol appears considerably more promising, particularly when compared with cellophane, polyisobutylene, Buna S and crude rubber, which produce severe irritation of the tissues.

Among the 252 animals operated on, only 1 death occurred directly as a result of hemorrhage in the liver—that in the animal in which a Buna S adhesive was used. While it is probable that the liver of the rat and rabbit possesses distinct limitation of bleeding properties, the present study appears to verify the previous observation that the synthetic resin (acrylic esters)—polyvinyl alcohol tape controls hemorrhage more satisfactorily than other adhesives investigated to date.

Dissolution of the synthetic adhesives, when it occurs, probably results from leukocytic and enzyme digestion, a process similar to the absorption of ordinary surgical gut. The essential innocuous properties of polyvinyl alcohol and acrylic esters in contact with living cells are demonstrated in the accompanying photomicrographs. Contrast the minimum adjacent tissue reaction in figures 1 to 11 with the marked



Fig. 1.—Liver of a rat ( $\times 40$ ) twelve weeks after pocket insertion of polyvinyl alcohol film. The plastic material is apparently being dissolved. Surrounding the thin-walled capsule is normal liver parenchyma. Darker-staining, regenerating hepatic cells are in evidence near the cut surface.

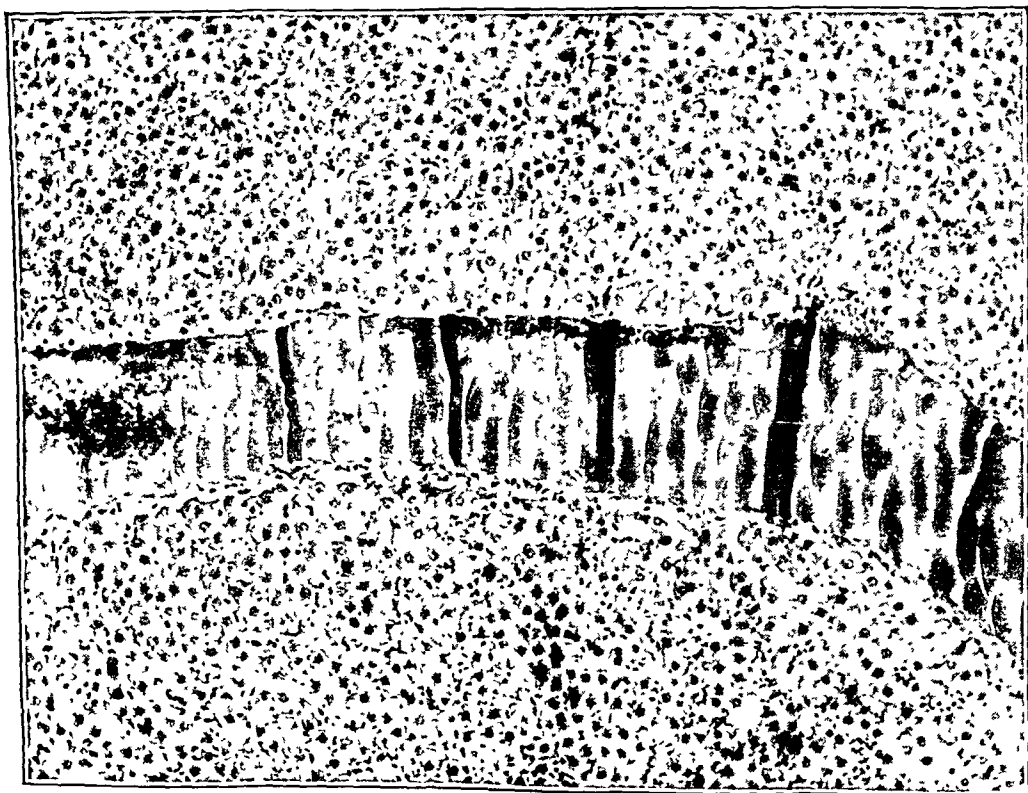


Fig. 2 ( $\times 140$ ).—High power magnification of different area from same rat as in figure 1 twelve weeks after implantation of polyvinyl alcohol film. Note absence of scar tissue reaction surrounding collagenous material, also normal structure of hepatic cells.



Fig. 3 ( $\times 175$ ).—Polyvinyl alcohol film implanted in pocket incision in liver of rat eighteen weeks previously. Two areas of scar remain separated by peninsula of liver tissue. Hepatic structure shows minimum damage.



Fig. 4 ( $\times 125$ ).—High power magnification of scar in figure 3 showing invasion of colloid material by leukocytes and fibrous tissue. Note healthy liver parenchyma adjacent to scar.



Fig. 5.—Spleen of rat ( $\times 27$ ) fourteen weeks after implanting polyvinyl alcohol film through sandwich incision. Note circular lighter zone of reaction engulfing well of disintegrating material. Lighter scar tissue area blends into apparently healthy splenic pulp.

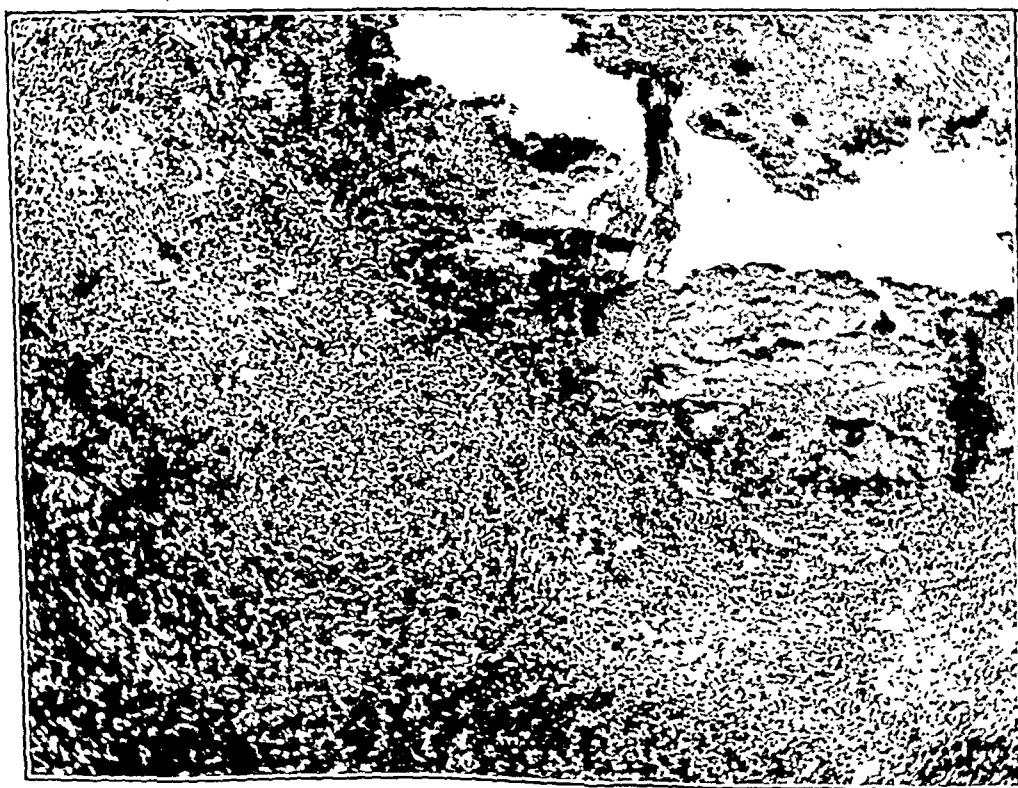


Fig. 6 ( $\times 85$ ).—High power magnification of figure 5. Colloidal material in stage of liquefaction is invaded by zone of leukocytes from surrounding splenic pulp.

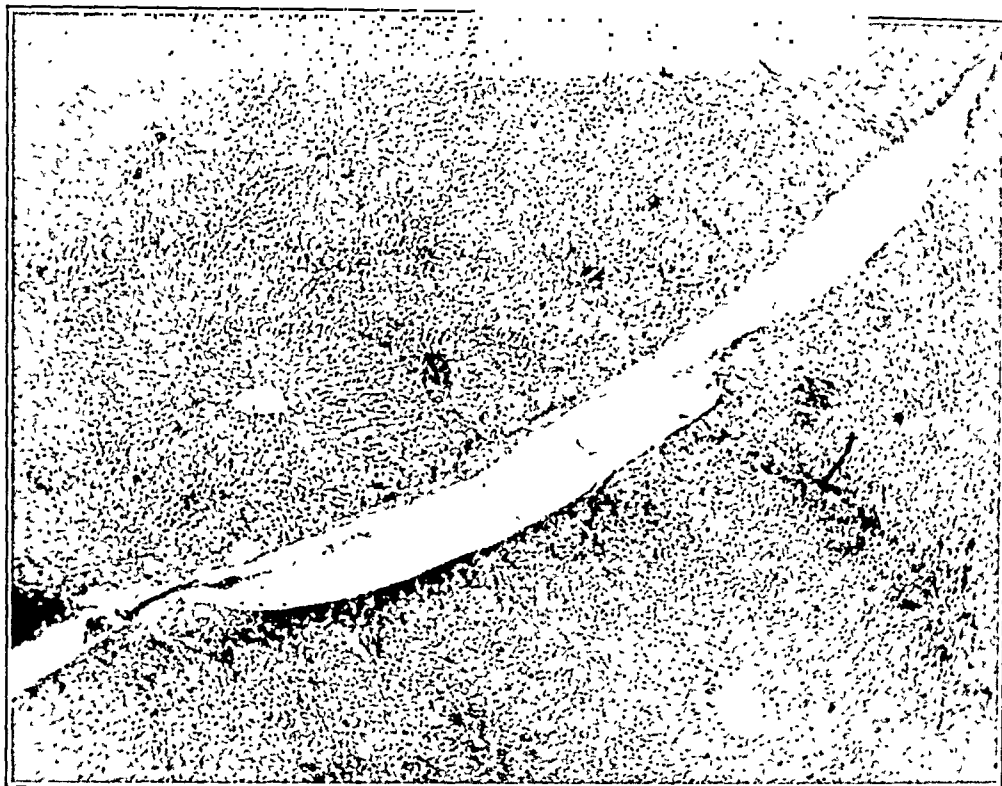


Fig. 7 ( $\times 40$ ).—Synthetic resin implant in liver pocket of rat eighteen weeks previously, showing cyst formation, with mild scar tissue capsule, blending immediately into undamaged liver parenchyma. The synthetic resin material itself is not seen.

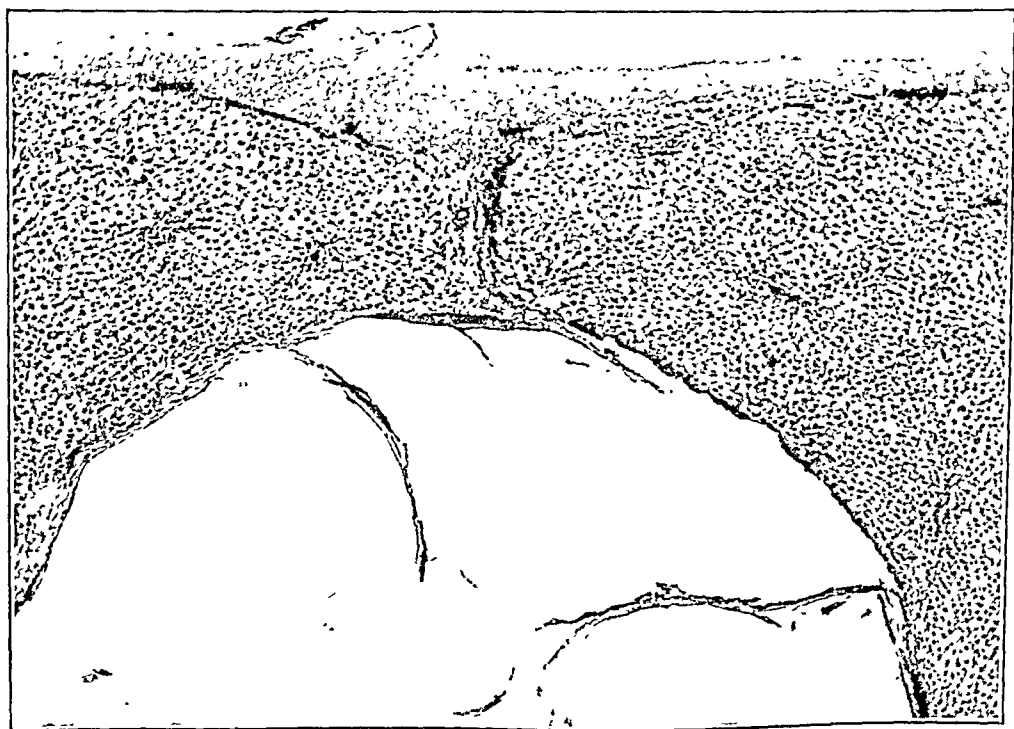


Fig. 8 ( $\times 50$ ).—Cyst resulting from implantation of large globule of synthetic resins in liver of rat fifteen weeks before; thin, scar tissue cyst capsule, with normal liver parenchyma immediately surrounding it. Note original incision scar in middle of hepatic tissue arch. Synthetic resins are not shown. Polyvinyl alcohol-synthetic resin tape has been on liver surface.





Fig. 9.—Spleen of rat six weeks after transverse incision of spleen and implantation of polyvinyl alcohol-synthetic resin tape, showing edge of cyst, in which tape had been rolled. Note considerable amount of hemosiderin, also small amount of scar tissue capsule in little-affected splenic pulp. Tape itself is not present.  $\times 90$ .

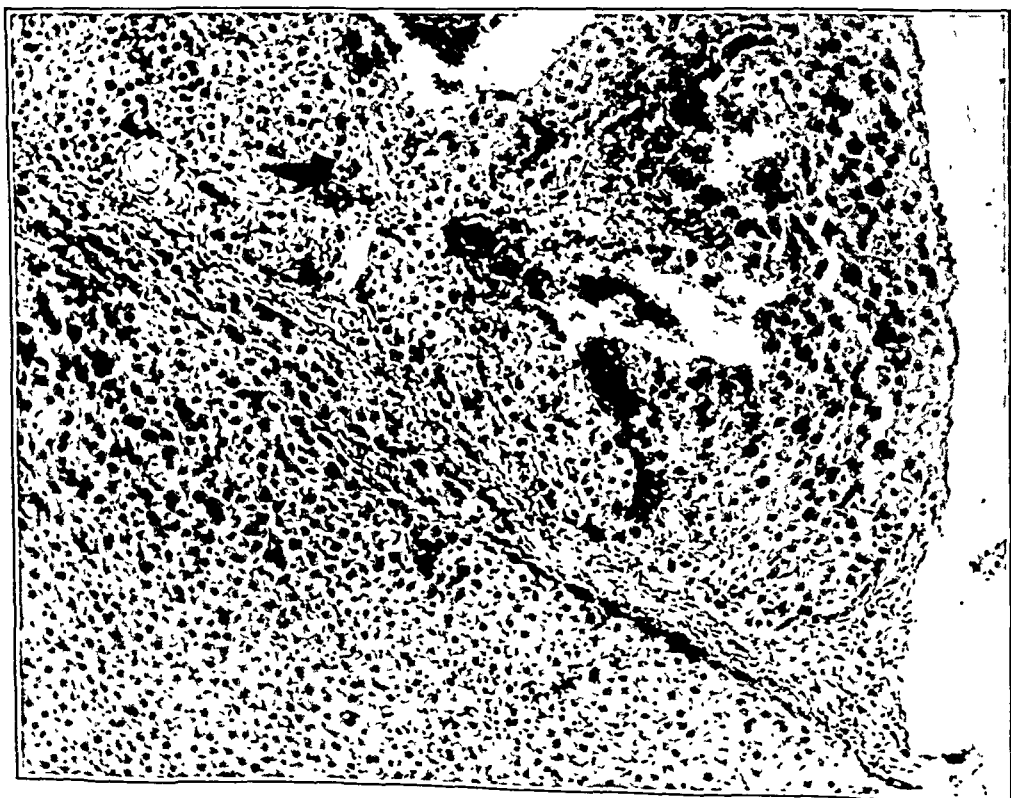


Fig. 10.—Liver of rate ( $\times 125$ ) sixteen weeks after pocket incision and embedding of polyvinyl alcohol film. Note dissolution of material, healed scar and adjacent normal hepatic parenchyma.



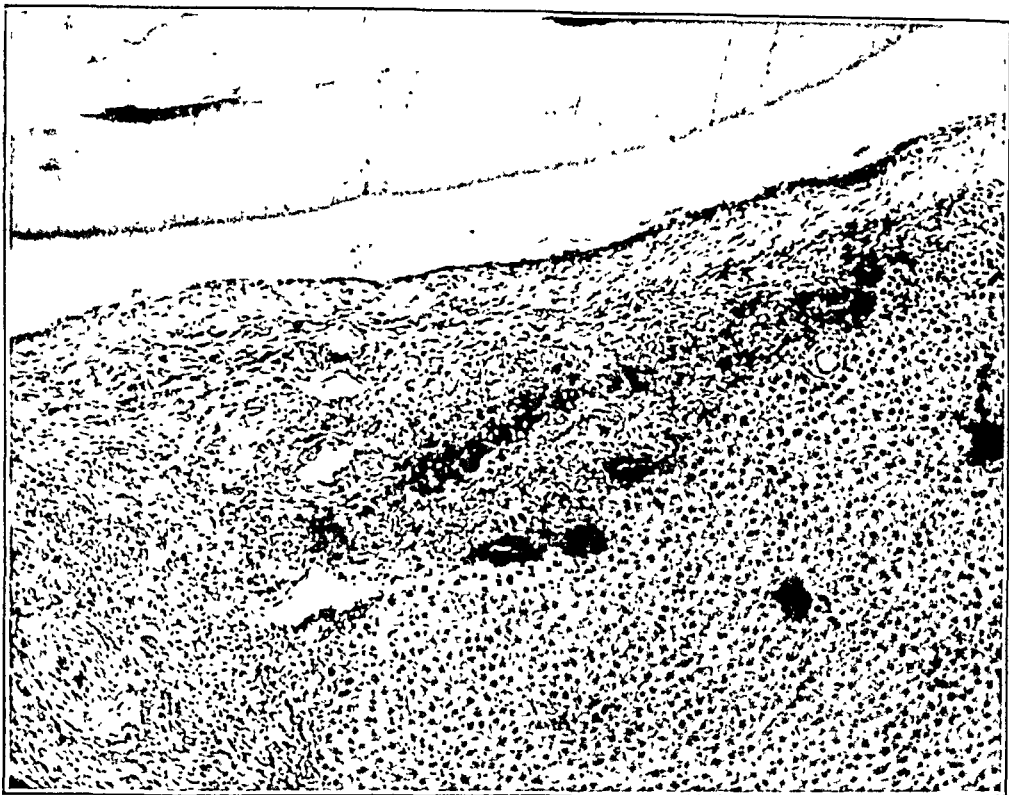


Fig. 11 ( $\times 85$ ).—Edge of liver cyst in rat, showing portion of undissolved polyvinyl alcohol film, which had been embedded in a tight roll fourteen weeks before. Though the scar tissue of this cyst is considerable, the immediate surrounding liver parenchyma is unaffected.

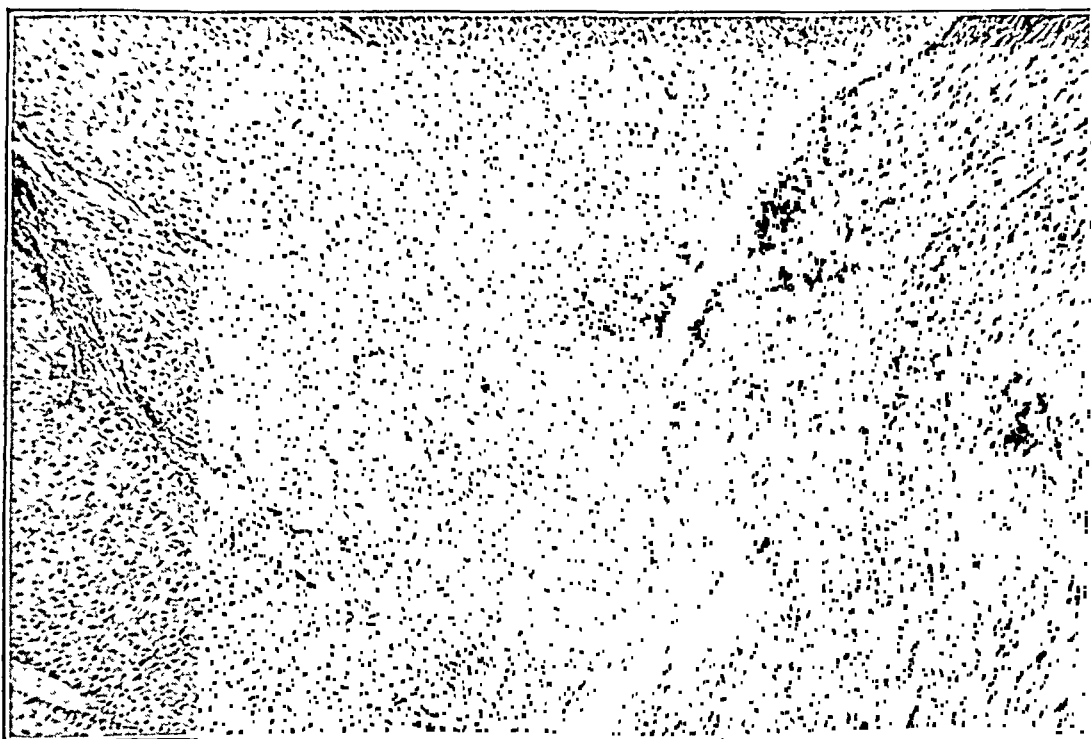


Fig. 12.—Cut of edge of liver of rabbit, with thick scar, from application seven weeks previously of a tape composed of polyisobutylene adhesive, rope stock and cellophane film. Note damage to cytoplasm of liver parenchyma. Contrast with tissue reactions after polyvinyl alcohol or synthetic resin.

inflammatory scar process in figure 12, a cellophane, rope stock, polyisobutylene tape application.

The main significance of the present report, it appears, lies not so much in the percentage of experimental animals in which the implanted synthetic adhesives are not found as in the demonstration that in some cases this plastic foreign body can apparently be absorbed by the tissue juices.

New tape structures and chemical combinations are being developed, in cooperation with the Minnesota Mining and Manufacturing Company, for further investigation. While these studies are additionally encouraging, it would be premature at this time to make such tapes available for surgical experimentation, a field offering unlimited scope for the application of a perfected, hemostatic and absorbable synthetic adhesive.

#### CONCLUSIONS

Hemorrhage of the liver in dogs, rats and rabbits, produced by surgical extirpation of a large section of the liver, can effectively be controlled by application of analogues in the plastic so-called Scotch tape. The most satisfactory synthetic adhesive, from the standpoint of adhesiveness, control of bleeding and minimum surrounding tissue reaction, is a recently developed transparent tape, consisting of a synthetic resin adhesive (acrylic esters) coated directly on to a polyvinyl alcohol film without an intervening paper binder.

After implantation of the component parts of this tape subcutaneously, intraperitoneally, within the liver and within the spleen, gross evidence of the inserted material could not be found in a percentage of the animals studied. The disappearance, or possible autolysis, occurs somewhat more often with polyvinyl alcohol film than with synthetic resin (acrylic esters). Intraperitoneal disappearance, or absorption, takes place oftener than with subcutaneous implants and apparently is influenced by the length of the time the material is in the body, its size and compactness and the avoidance of infection. Microscopic sections of the liver and spleen reveal the possibility of the polyvinyl alcohol film being absorbed with little scar formation and practically no parenchymal damage. Synthetic resin (acrylic esters) inserts, while nontoxic to tissue, have a tendency, in a compact mass, to cause cyst formation and somewhat more scar formation.

It is not unreasonable to presume that a synthetic adhesive tape, hemostatic, nonirritant to tissues and capable of absorption, can be developed. The manifold possibilities of this perfected tape reveal themselves in all surgical fields. Further animal investigation with

analogous adhesive structures (now in progress), together with a satisfactory method of sterilization, is necessary before these synthetic adhesives are ready for clinical trial.

#### SUMMARY

1. Ten rabbits and 7 dogs had sections of their livers removed and the gap closed above and below in a plastic adhesive envelope of various analogues of Scotch tape. One rabbit died of hemorrhage and 1 of peritonitis; the rest of the animals recovered and were subjected to autopsy, one to seven weeks later. Reactions in the liver varied from intrahepatic abscess with an undissolved foreign body to a mild fibrous scar, depending on the type of synthetic adhesives used. A tape composed of a synthetic resin (acrylic esters) adhesive on a polyvinyl alcohol film without a paper binder caused the minimum of tissue reaction. At the end of four weeks none of these tapes had dissolved in the test tube either in human gastric juice or in human blood serum.

2. Of 10 control rodents with no synthetic adhesives over the sectioned liver, 6 succumbed one hour after abdominal closure and 2 within four hours; another died ten hours later and 1 animal recovered.

3. In a series of 235 animals (rabbits, mice and rats) the synthetic resins (acrylic esters), the polyvinyl alcohol film and the synthetic adhesive tape combination (the two plastics together) were separately implanted within the liver, within the spleen, intra-abdominally and subcutaneously. At intervals from one week to eight months later the recovered animals were subjected to autopsy and the tissues studied microscopically.

The number of animals in which the synthetic resin was not found was 17 per cent for the subcutaneous application and 26 per cent for application within the peritoneum (average for liver, spleen and intra-abdominal implants). With polyvinyl alcohol film inserts, the numbers were 17 and 43 per cent. For the combined polyvinyl alcohol-synthetic resin tape the percentages were 28 and 38.

Microscopic sections revealed no decided parenchymal damage in the liver or spleen from synthetic resin or polyvinyl alcohol implants. Scar tissue reaction was minimum, particularly with polyvinyl alcohol, although cyst formation was found with compact synthetic resin inserts. In numerous cases the material seemed to have been dissolved.

Factors apparently influencing absorption are size, weight and compactness of inserts, length of time, place of implant and avoidance of infection.

4. Sterilization of the tape may be accomplished by ultraviolet irradiation rather than autoclaving.

5. While the present synthetic resin-polyvinyl alcohol plastic tape cannot yet be recommended for clinical studies in man, there are encouraging probabilities for the early development of a satisfactory synthetic adhesive tape hemostatic, nonirritating to tissues and completely absorbable within the body.

Many officers and enlisted men of the United States Army and Navy Medical Corps and members of the University of Utah, University of Oregon and the University of Southern California Medical Schools assisted in this work.

Part of the study was carried on in the laboratories of the Department of Pharmacology and Toxicology, University of Southern California Medical School.

# MULTIPLE PRIMARY TUMORS WITH FIBROSARCOMA AND COEXISTING CARCINOMA OF THE LUNG

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THE INCIDENCE of multiple primary tumors is low. Slaughter,<sup>1</sup> confirming the impression of Warren and Gates,<sup>2</sup> stated that cases of multiple primary malignant growths represent 3.9 per cent of all cases of cancer. Primary sarcoma of the lung constituting one of these tumors is even less common. Primary carcinoma of the lung, on the other hand, is by no means an uncommon disease—constituting about 10 per cent of all cases of cancer seen at necropsy—and is occasionally seen in instances in which two primary cancers coexist in the same person. The occurrence of a primary carcinoma of the lung in a patient who has a primary sarcoma of that organ with another benign tumor of the contralateral lung is extremely rare. It is even rarer to find such a state further complicated by several benign tumors in other organs.<sup>3</sup> The case to be reported is an example of multiple neoplastic tumors.

## REPORT OF A CASE

I. S., a 55 year old white woman entered The Jewish Hospital of Brooklyn on Aug. 19, 1947, complaining of a chronic cough of ten years' duration. In recent months the cough had become more severe and more disturbing, especially during the early part of the day. About four months prior to the patient's admission to the hospital the sputum became streaked with blood. This gradually subsided and was followed by a change from the heretofore nonproductive cough to one productive of a mucoid sputum, which later became mucopurulent in

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From the departments of thoracic surgery and pathology, Jewish Hospital of Brooklyn.

1. Slaughter, D. P.: The Multiplicity of Origin of Multiple Tumors, *Internat. Abstr. Surg.* **79**:89, 1944.

2. Warren, S., and Gates, O.: Multiple Primary Malignant Tumors, *Am. J. Cancer* **16**:1358, 1932.

3. Hochberg, L. A.: Primary Carcinoma of the Lung, to be published.

character. A roentgenogram of the chest taken one week before her entrance to the hospital revealed a "well circumscribed opacity of the left upper lobe," interpreted as a "lung cyst or a degenerative process." The patient's past history was not remarkable, except for a hysterectomy in 1945 for "fibroids of the uterus."

Examination revealed an apparently healthy vigorous middle-aged woman, whose blood pressure was 132 systolic and 88 diastolic and whose temperature, pulse and respirations were normal. On the abdomen there was a well healed

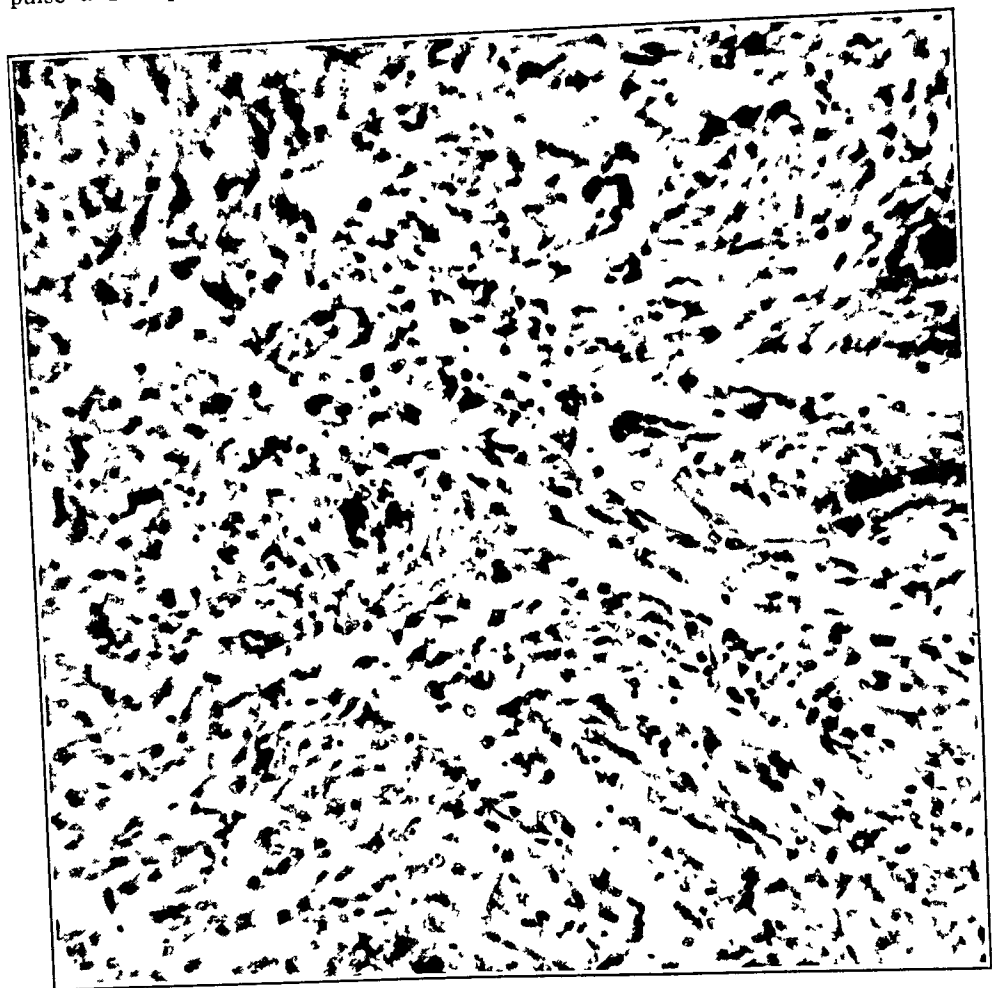


Fig. 1.—Fibrosarcoma of the lung ( $\times 200$ ).

right suprapubic scar. There was some dullness to percussion over the upper third of the left side of the chest posteriorly, in which region the breath sounds were absent, especially opposite the second dorsal vertebra. The examination was otherwise noncontributory.

A roentgenogram of the chest was interpreted as containing a "circular tumor involving the upper half of the left lung field . . . possibly not a bronchogenic carcinoma but one of the neurofibromatous group . . ."

The hemoglobin content was 90 per cent, the red blood cell count 4,420,000, and the white blood cell count 11,450, with a differential count of 65 per cent

polymorphonuclear cells, 8 per cent band cells, 7 per cent lymphocytes, 19 per cent eosinophils and 1 per cent monocytes. The sedimentation rate was 10 mm. in an hour. Urinalysis showed a faint trace of albumin and an occasional white blood cell per high power field. The blood urea nitrogen was 17.8 mg. per hundred cubic centimeters, and the blood sugar was 112 mg. The reaction to the Kline test was negative. The sputum contained *Streptococcus viridans*, *Micrococcus catarrhalis* and diphtheroids. Tubercle bacilli were not present in the sputum. The electrocardiogram was within normal limits.

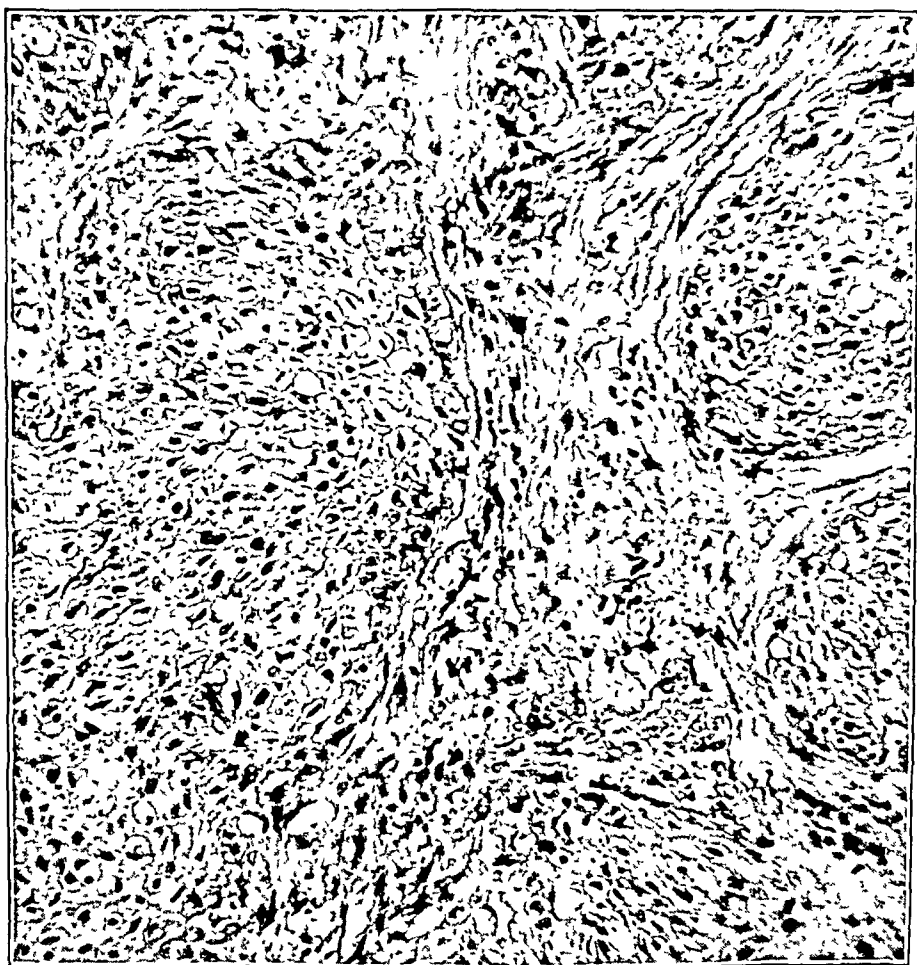


Fig. 2.—Fibrosarcoma of the lung with coexisting epidermoid carcinoma ( $\times 200$ ).

On August 22, the third hospital day, thoracotomy was performed on the left side under general anesthesia. A large mass was found in the upper lobe. The neoplasm was attached to the anterior wall of the chest and to a lesser extent to the distal part of the transverse part of the aorta. There were no nodes in the mediastinum. The upper lobe of the left lung was removed by individual ligation and suture of the vessels and bronchus. During the operation the blood pressure and pulse rate varied considerably, but they were essentially

normal at the end of the procedure. At no time was there any impairment of respiration. When the patient was returned to her room, the blood pressure, pulse and respiratory rate were not remarkable. However, she did not regain consciousness. The transfusion started during the operative procedure was continued in the patient's room. About five hours after the patient was returned to her room she was still unconscious, breathing with some difficulty. About 11 p. m. (twelve hours postoperatively) she was still unconscious, the temperature was 104.2 F. and the respirations were easier and regular. Five hours later the

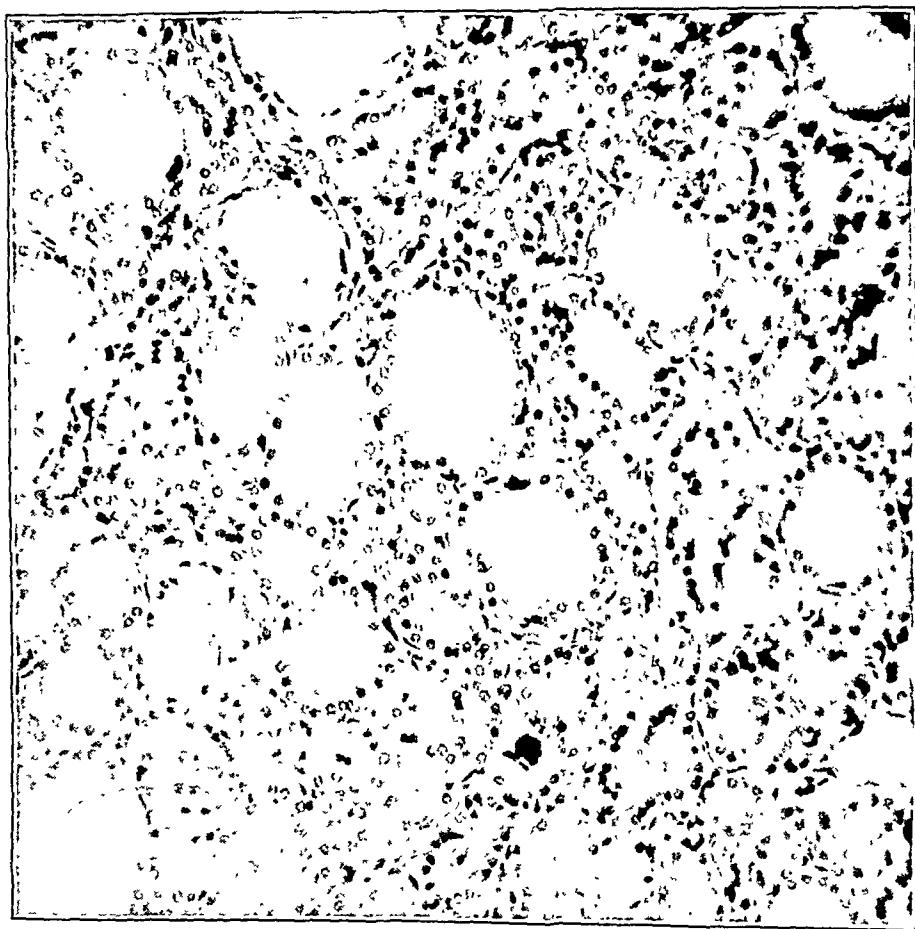


Fig. 3.—Colloid adenoma of the thyroid ( $\times 200$ ).

temperature rose to 106.4 F., the pulse rate rose to 140 per minute and was thready and the respiratory rate rose to 52 per minute and occasionally was Cheyne-Stokes in character. The patient died seventeen hours after completion of the operation never regaining consciousness.

*Surgical Specimen.*—The surgical specimen consisted of the upper lobe of the left lung. It was pinkish gray, measuring 23.0 by 11.5 by 6.0 cm. It was soft and noncrepitant. Projecting above the surface and within the substance of the lung there was a firm, pinkish yellow irregular mass 11.5 by 10.0 by 5.0 cm., which was sharply demarcated from the adjacent lung tissue. The cut surface



of the mass was soft and yellowish pink, with a hemorrhagic center. A secondary bronchus could be seen leading into the tumor mass. Tumor tissue was also present in the large veins. Microscopic examination of the mass showed a varied picture. The tumor consisted of spindle-shaped cells, varying in size, with ovoid or round vesicular nuclei; some of the cells were hyperchromatic, and an occasional cell was in mitotic division. The cells were arranged in intertwining bands or in whorls. The stroma was vascular and contained many foci of extravasated blood. With Laidlow connective tissue and Mallory stains, the tumor

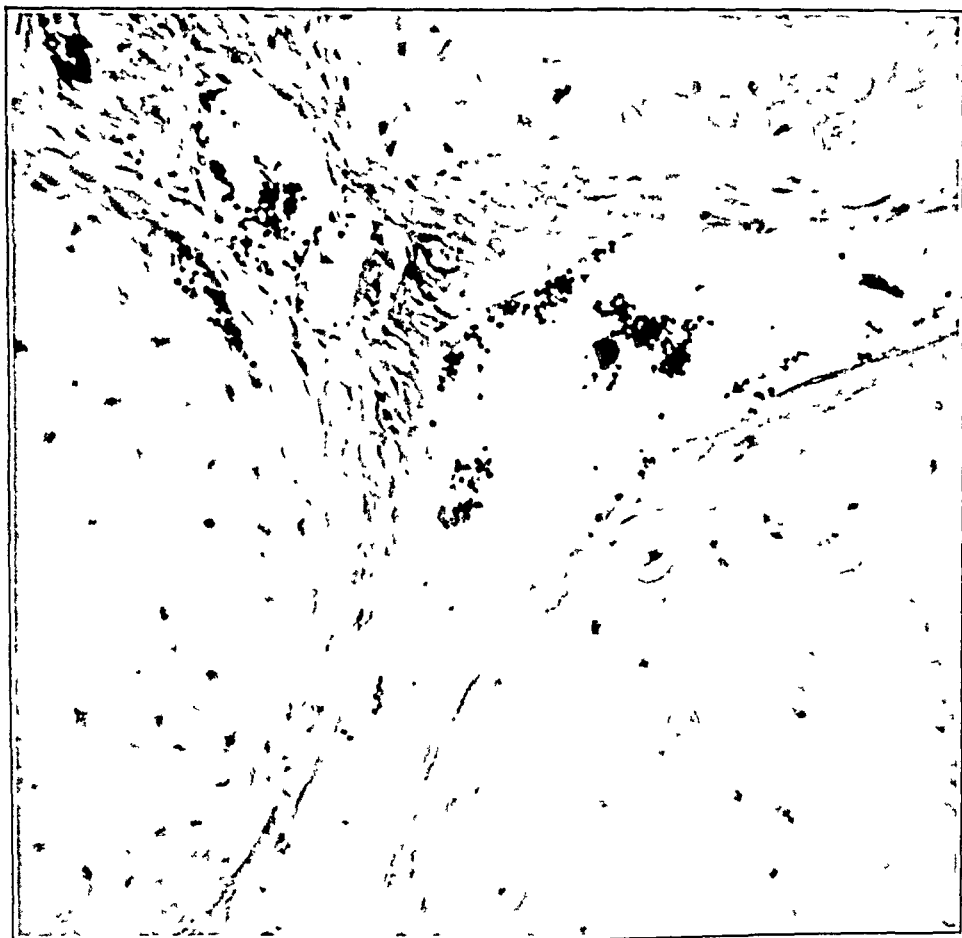


Fig. 4.—Chondroma of lung ( $\times 200$ ).

was seen to contain a great deal of collagen arranged in dense bands in some areas and in a fibrillary fashion in others. Intermingled with these cells there were nests of large ovoid or polygonal cells of varying size and shape. Some of these cells were seen within endothelium-lined spaces.

*Diagnosis.*—The diagnosis was fibrosarcoma and carcinoma of the upper lobe of the left lung (figs. 1 and 2).

*Observations at Autopsy.*—The body was that of a well developed, obese, middle-aged white woman. A 30 cm. semilunar recent surgical incision was present on the left hemithorax, extending along the sixth rib from the costochondral junction

to the vertebra. A 13 cm. old right rectus scar was present in the lower part of the abdomen. About 100 cc. of dark red blood was present in the left pleural cavity. The hilar vessels were snugly tied, and the remains of the bronchus to the upper lobe of the left lung were closed securely by several interrupted black silk sutures. The edge of the liver projected 8 and 4 cm. below the right and midcostal margins respectively.

The thyroid contained a small firm yellowish nodule at the periphery. On cut section it was yellowish and faintly lobulated, measuring 1.1 cm. in diameter.

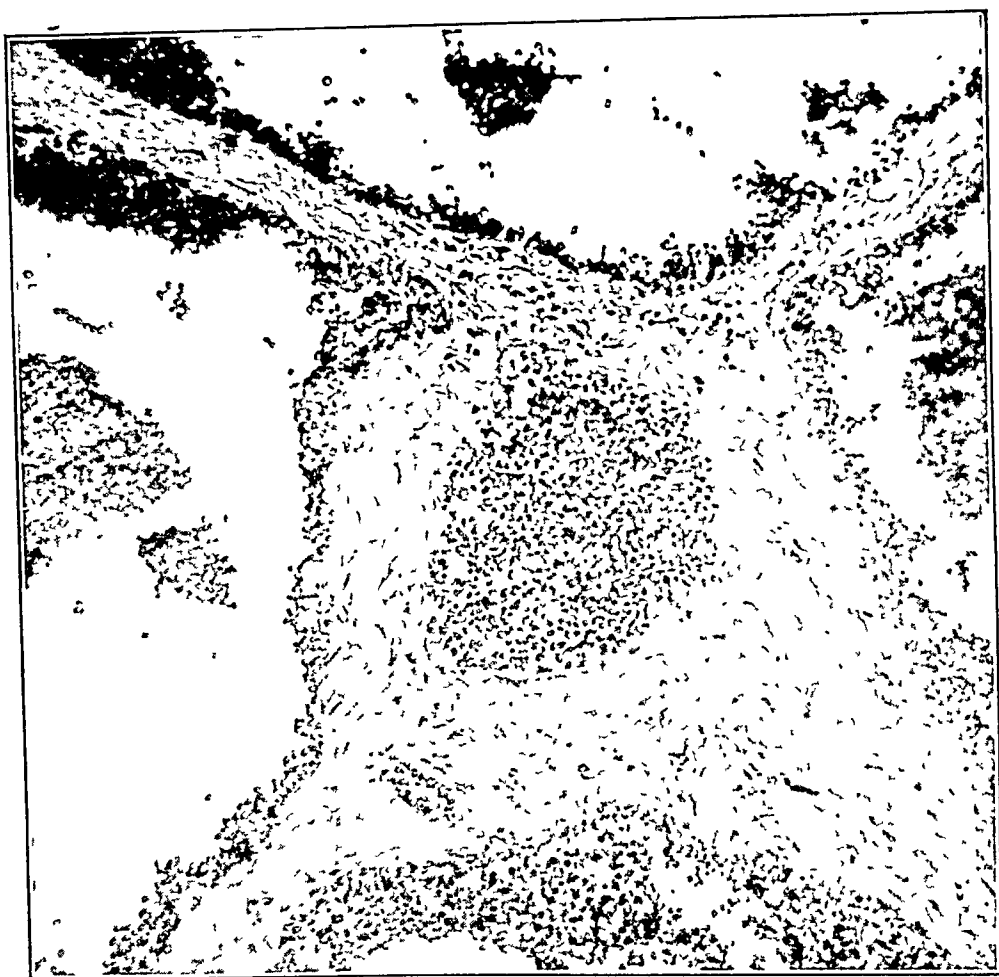


FIG. 5.—Cavernous hemangioma of liver ( $\times 200$ ).

Microscopically this nodule consisted of several discrete, well circumscribed oval masses of thyroid tissue in which the colloid took a dark pink stain and the acini were small and rudimentary (fig. 3). The remainder of the gland was not unusual.

The right lung weighed 423 Gm and was well aerated. A hard white firm nodule, 2.1 cm in diameter, was present at the periphery of the middle lobe. On section this nodule was gray-white and delineated from the surrounding parenchyma. Microscopic examination revealed irregular masses of light pink and

dark purple cartilaginous tissue having poorly stained nuclei. Separating these cartilaginous areas were thin and broad areas of adipose tissue, primitive cuboidal cell-lined ducts with many desquamated lining cells, loose mucoid tissue with many fibroblasts and light pink hyaline zones and many congested thin-walled vessels (fig. 4).

The liver weighed 2,240 Gm. At its extreme right and on the diaphragmatic surface there was a large dark blue lobulated area, 9.0 by 11.0 by 5.0 cm., which on section consisted of dark-bluish red areas traversed by thick white fibrous

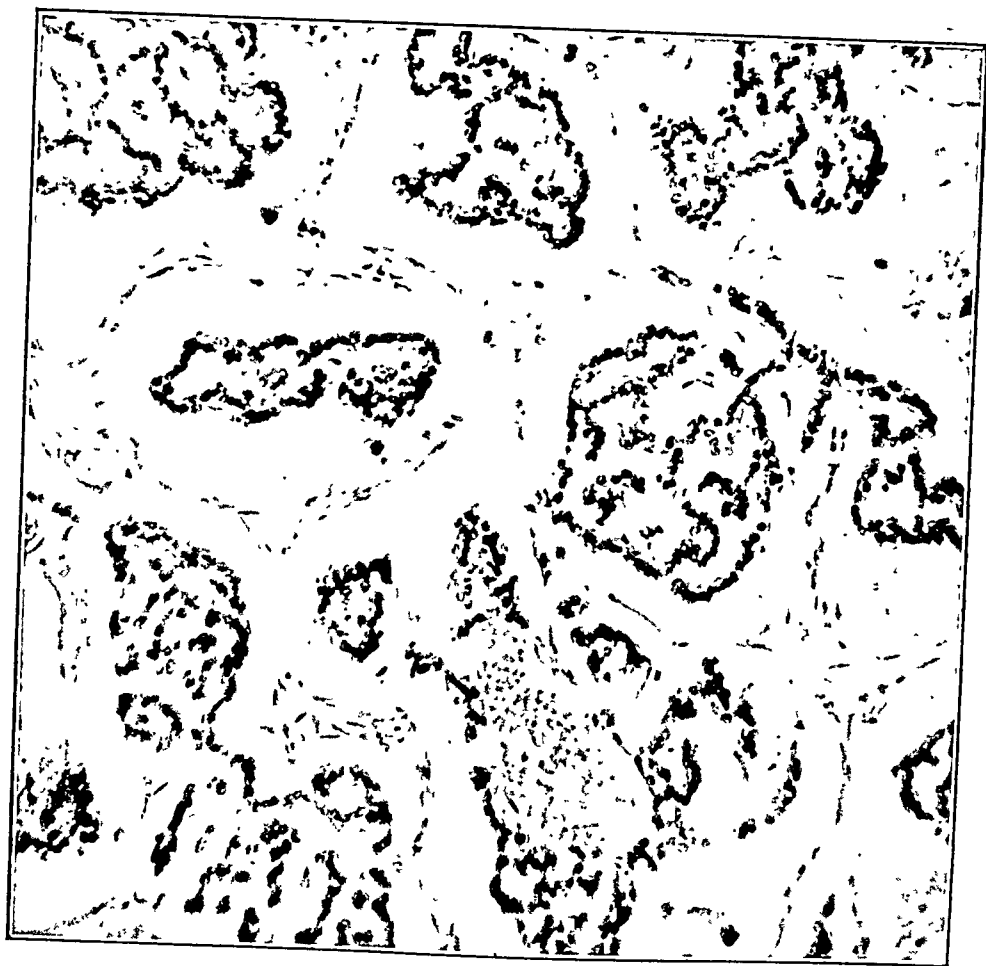


Fig. 6.—Nesidioblastoma of pancreas ( $\times 200$ ).

strands. A similar, although smaller, area was found at the posterolateral extremity of the left lobe of the liver. Microscopic examination of these two areas showed large and small irregular cystic spaces, congested with lymphocytes and lined by prominent endothelium. Separating the cystic spaces were broad septums composed of loose collagenous tissue with many areas of hyalinization (fig. 5). The zones were distinctly demarcated from the hepatic parenchyma.

The pancreas weighed 150 Gm. and grossly was not remarkable. Microscopic examination, however, revealed an isolated, well encapsulated zone of atypical tissue within otherwise normal pancreas. This tissue had a loose light pink

reticulum encompassing vacuolated spaces in which could be seen irregular cords, in linear arrangement, containing dark-staining nuclei and light purple homogeneous cytoplasm (fig 6). Many cords had united to form glandular structures which showed hyperplasia of the epithelial lining.

The spleen weighed 365 Gm. At the periphery there was a dark bluish area, 2 cm. in diameter, which was firmer than the adjacent splenic tissue and distinctly demarcated from it. Microscopically this tissue consisted of cystic spaces containing a dark homogeneous material and many erythrocytes. The lining of these

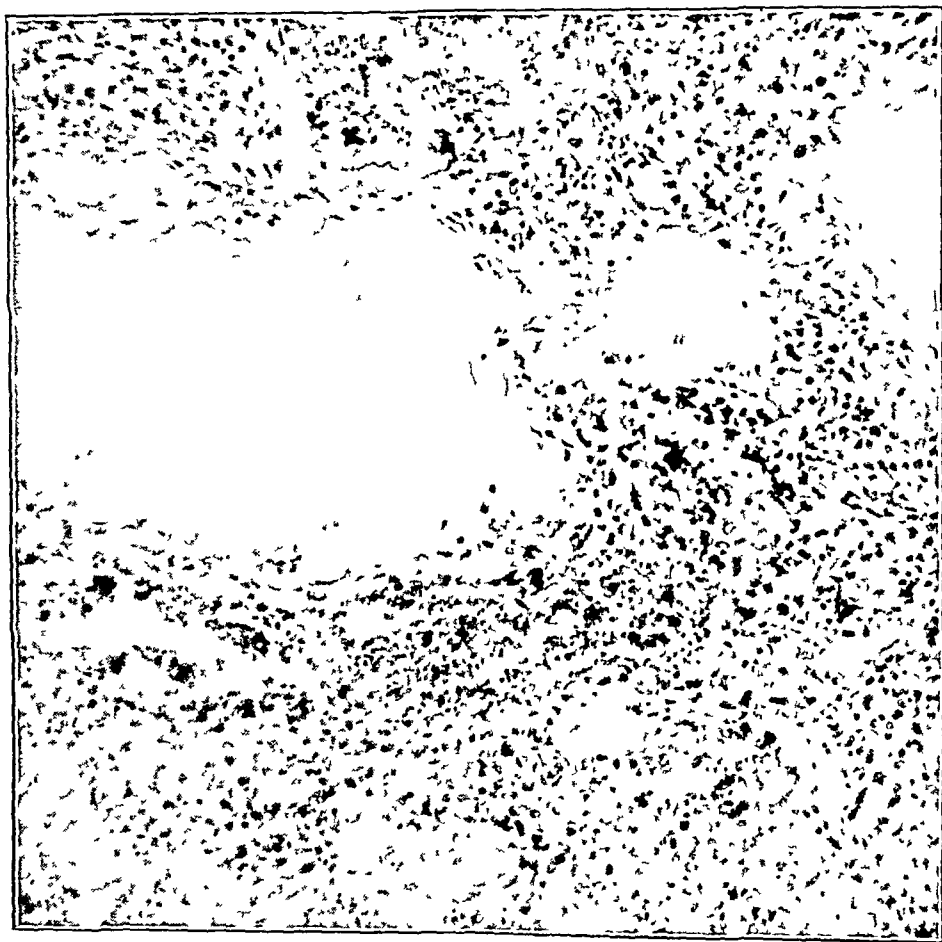


Fig. 7.—Cavernous hemangioma of spleen ( $\times 200$ ).

spaces was not clearly defined (fig 7). The cystic tissue merged gradually with the normal splenic tissue. One vessel within the spleen contained a prominent tumor thrombus consisting of fibrosarcomatous elements.

The right adrenal gland presented nothing unusual. The left adrenal gland was almost completely replaced by fibrosarcomatous tissue.

Both kidneys presented severe nephrosis and contained fibrosarcomatous thrombi in many arteries.

Tumor thrombi were also found in the left internal carotid and left middle cerebral arteries.

Examination of the slides of the uterus removed two years previously showed leiomyomas (fig. 8). There was no evidence of cancer in any of the slides.

*Anatomic Diagnosis.*—The anatomic diagnosis was as follows: Excision of the upper lobe of the left lung; fibrosarcoma and carcinoma of the lung; fibrosarcomatous metastasis to adrenal gland and left periadrenal tissue; fibrosarcomatous thrombi in the arteries of the spleen, kidneys and brain; arteriosclerosis of cerebral vessels with recent tumor thrombi in the left internal carotid and left middle

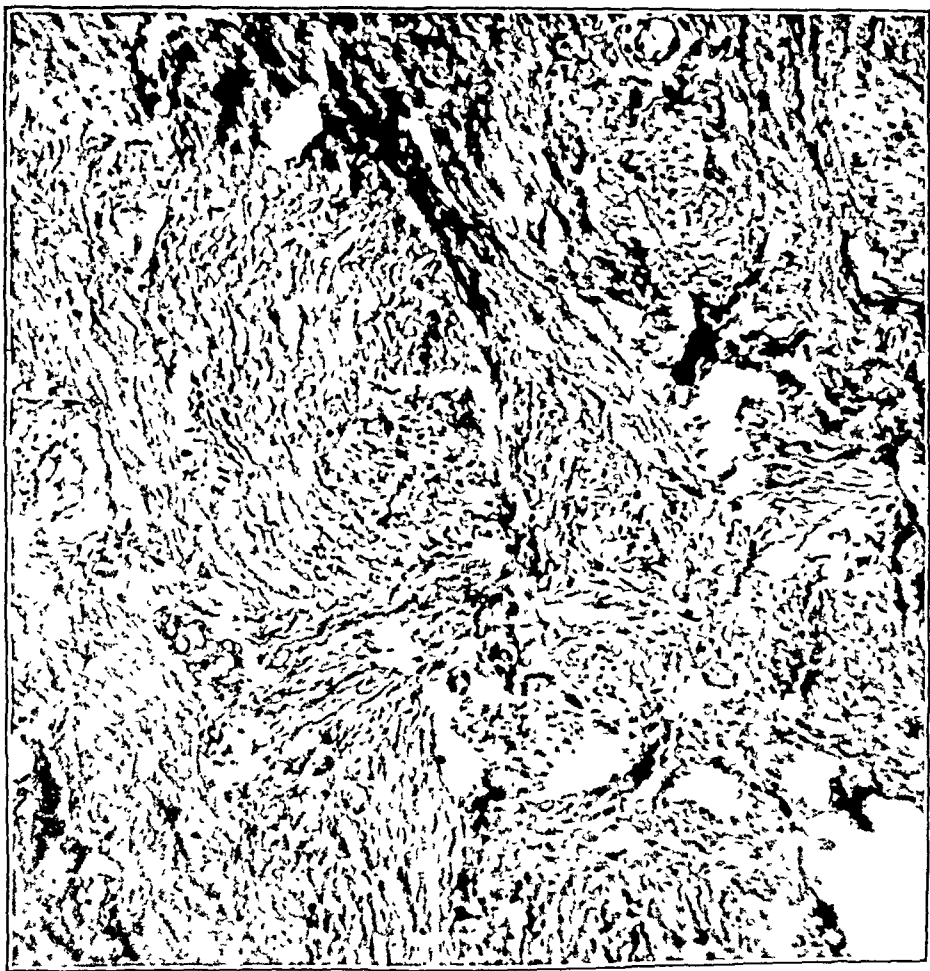


Fig. 8.—Leiomyomas of uterus ( $\times 200$ ).

cerebral arteries; recent infarction of the left internal capsule, left globus pallidus and pons; hepatitis and cirrhosis of the liver; nephrosis; edema of the brain; congestion of the viscera; chronic pneumonitis of the right lung; arterial nephrosclerosis; colloidal adenoma in the thyroid; chondroma in the right lung; cavernous hemangiomas of the liver; cavernous hemangioma in the spleen; nesidioblastoma of the pancreas; diverticula and adenomatous polyp of the descending colon; scar of hysterectomy [for leiomyomata uteri] with fibrous peritoneal adhesions, and follicular cysts in the right ovary.

SUMMARY

An unusual case of multiple tumors is presented. Besides carcinoma and fibrosarcoma of the left lung, tumors were found in six organs. Five of the benign lesions were asymptomatic, and the sixth gave rise to symptoms necessitating a hysterectomy. The malignant tumor gave rise to symptoms requiring a pulmonary lobectomy.

The susceptibility to tumor formation exhibited by this patient seemed to be more than a mere coincidence. Perhaps she truly was endowed with a "tumor diathesis."

# INTRA-ARTERIAL ADMINISTRATION OF PENICILLIN WITH SPECIAL REFERENCE TO BONE MARROW CONCENTRATION

An Experimental Study

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THE RATIONALE of the intra-arterial injection of antiseptic substances was formulated by Parlavecchio<sup>1</sup> in 1899. From his experimental observations he concluded that the procedure was a feasible method of obtaining a high concentration of therapeutic agent in a diseased tissue. In his report he suggested that the presence of a peripheral capillary field, in addition to the pulmonary circuit, through which a substance so injected must pass before it could reach the brain and other viscera, tended to minimize any toxic effect.

These assumptions have formed the logical basis for the sporadic clinical reports that have since appeared. The advent of penicillin served as a stimulus to trial of this technic. In 1944, Ribeiro<sup>2</sup> treated a patient with purulent osteoarthritis of the knee by repeated injections into the femoral artery. At the same time, Gudín and Neiva Filho<sup>3</sup> successfully treated 2 patients with osteomyelitis who previously had not responded to intramuscular administration of penicillin. In 1945, Glasser and associates<sup>4</sup> and, in 1946, Shaffer<sup>5</sup> reported the effects of arterially injected penicillin on inflammatory and vascular processes of the extremities.

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From the Division of Bacteriology, Laboratories of the Mount Sinai Hospital.

1. Parlavecchio, G.: *Sul lavaggio antisettico interstiziale dei tessuti dalla via arteriosa, Policlinico (sez. prat.)* 6:66-74 (Feb.) 1899.

2. Ribeiro, E. B.: *Penicilina por via arterial, Bol. San. São Lucas* 6:19-20 (Aug.) 1944.

3. Gudín, M., and Neiva Filho, A.: *Tratamento da osteomielite por asepsia integral e penicilina intra-arterial, Mem. Inst. Oswaldo Cruz* 41:163-166 (Aug.) 1944.

4. Glasser, S. T.; Herrlin, J., and Pollock, B.: *Intra-Arterial Injection of Penicillin for Infections of the Extremities, J. A. M. A.* 128:796-802 (July 14) 1945.

5. Shaffer, J. O.: *Intra-Arterial Penicillin Therapy for Infections of the Extremities, Minnesota Med.* 29:928-932 (Sept.) 1946.

While these clinical experiences imply confirmation of the principles involved, there is lacking a quantitative estimation of the concentration of penicillin in the tissues after the injections. The experiments reported here were designed to study the comparative local levels of penicillin after various methods of administration. Because of its clinical significance, bone marrow was the tissue selected for assay.

#### EXPERIMENTAL STUDY

Young male dogs were employed throughout, with the exception of 2 older dogs to be noted later. The animals were anesthetized by the intravenous injection of veterinary pentobarbital sodium. The dose was 0.5 cc. per kilogram of body weight, and if necessary more was administered during the operation.

*Operation.*—The tibia and femur of one side were exposed, great care being exercised not to injure the nutrient arteries of the bones. The cortical layer of the presenting surfaces was then chiseled off. Free bleeding, indicating an intact blood supply, was noted in the marrow cavity. The femoral artery on the same side was isolated for injection. Commercial penicillin, 10,000 units per cubic centimeter in isotonic solution of sodium chloride, was injected in the amounts and by the routes and methods indicated in the tables. The intravenous injections were made into the ear vein and the intramuscular injections were given into the pectoral muscle. The intra-arterial injections were made into the femoral artery on the same side as the exposed bones, under direct vision in order for us to be certain that the entire amount was delivered into the lumen. After the intra-arterial injection, bleeding stopped almost immediately after slight pressure, provided that the femoral artery was not denuded of its sheath. When two injections were given, either a twenty or a thirty minute interval was allowed, as indicated in table 2.

Specimens of bone marrow were obtained at the periods indicated. Immediately before the specimens were taken by means of a mastoid curet, bleeding in the marrow cavity was momentarily stopped by compression with dry gauze. We were extremely careful to procure true bone marrow, rather than clotted blood or seepage, for penicillin assay. One half of each specimen was from the femur and the rest from the tibia, so that each specimen represented combined femoral and tibial marrow. The first specimen was taken from the central portion of the marrow cavity, and subsequent periodic samples were obtained from sites in a progression toward the epiphysial plate in order that the vascular architecture and blood supply of the later specimens should be disturbed as little as possible.

The operation and the collection of specimens were performed under strictly aseptic conditions.

*Penicillin Assays.*—Each specimen of bone marrow was suspended in distilled water in a concentration of 50 mg. per cubic centimeter. After the marrow had been crushed by means of a solid glass rod, the samples were controlled for sterility in a 1 per cent dextrose broth containing penicillinase and were placed in the freezing compartment of the refrigerator overnight. Contaminated specimens were filtered through a Seitz filter. The following day, after being permitted to thaw out, the marrow suspensions were agitated vigorously and then centrifuged at 3,000 revolutions per minute for twenty minutes. Assays for penicillin were made on the supernatant fluids.



The method employed in this laboratory is a broth tube dilution method with *Staphylococcus aureus* H used as the test organism and fresh meat extract broth as the medium. The minimal concentration of the standard penicillin required to inhibit the inoculum of  $5 \times 10^2$  *Staph. aureus* H cells was 0.02 unit

TABLE 1.—*Levels of Penicillin in the Bone Marrow of Dogs After Single Injections of Penicillin by Various Routes*

Dog	Weight (Kg.)	Route of Administration	Dose (Units/Kg.)	Levels of Penicillin in Bone Marrow (Units/Gm.)					
				10 Min.	20 Min.	30 Min.	60 Min.	120 Min.	180 Min.
1	19.2	Intra-arterial	2,000	4.0	...	2.0	0.8	<0.8	0.8
2	12.5		2,000	1.32	0.8	0.88	0.8	<0.8	...
*3	14.5		2,000	2.0	0.5	<0.5	1.3	...	...
*4	22.0		4,000	4.0	4.0	4.0	2.0	2.0	<0.8
5	15.0		4,000	8.0	...	1.98	1.0	...	...
1	19.2	Intravenous	2,000	2.0	<0.8	...	<0.8	...	...
6	9.2		2,000	10.0	1.32	1.0	1.0	1.0	...
7	16.0		2,000	0.5	<0.4	...	0.5	...	...
*8	15.6		4,000	1.0	1.0	0.8	<0.8	<0.8	<0.8
*9	14.5		4,000	<0.8	0.8	0.8	<0.8	<0.8	0.8
*10	14.2	Intramuscular	4,000	10.0	8.0	2.0	<0.8	0.8	...
*11	14.6		4,000	0.8	4.0	2.0	0.8	...	...
*12	12.2		4,000	1.0	4.0	<1.0	<1.0	...	...
*16	10.6		4,000	<1.0	<1.0	1.14	1.0	...	...
17	11.8		4,000	1.0	0.8	<1.0	1.0	...	...

\* Refer to table 2.

TABLE 2.—*Levels of Penicillin in the Bone Marrow of Dogs After Two Injections of Penicillin by Various Routes, 2,000 Units per Kilogram of Weight Being Given at Each Injection*

Dog	Weight (Kg.)	Route of Administration	Levels of Penicillin in Bone Marrow (Units/Gm.)								
			10 Min.	20 Min.	30 Min.	40 Min.	50 Min.	60 Min.	80 Min.	90 Min.	150 Min.
*4	26.0	Intravenous	2.0	4.0	1.14	↓8.0	4.0	4.0	...	...	2.0
15	18.7	and	<0.5	<0.5	↓2.0	1.0	<0.5	...	<0.5	...	...
*12	11.6	Intravenous	2.6	1.6	↓4.0	...	1.32	...	1.0	...	...
		Intramuscular									
*16	10.5	and	1.98	<1.32	↓<1.0	<1.0	...	...	...	...	...
18	10.2	Intra-arterial	<1.0	<1.0	↓<1.0	<1.0	1.0	...	<1.0	...	...
*8	19.0		2.0	0.8	1.0	↓4.0	...	1.32	...	<0.8	<0.8
*10	14.0	Intra-arterial	4.0	4.0	0.88	↓13.2	4.0	0.8	...	0.8	<0.8
*9	14.5	and	<0.8	<0.8	...	↓<0.8	<0.8	...	...	...	<0.8
13	20.0	Intra-arterial	4.0	4.0	↓10.0	...	1.0	...	1.0	...	...
14	8.5		<1.0	<1.5	↓8.0	<1.0	...	...	...	...	...
19	12.3		0.8	1.32	...	↓13.2	10.0	...	...	...	...
20	15.7	Intravenous	4.0	2.0	0.8	↓10.0	4.0	2.0	...	2.0	1.32
*11	14.5	and	0.88	<0.8	0.88	↓13.3	6.65	<0.88	...	1.44	0.88
*3	13.3	Intra-arterial	4.0	1.32	↓16.0	8.0	<1.0	...	...	...	...
21	9.7		<1.0	1.32	↓11.4	4.0	1.14	...	<1.0	...	...
18	9.6		<1.0	<1.0	↓8.0	2.6	<1.0	...	...	...	...

\* Refer to table 1.

↓ Indicates time of second injection.

per cubic centimeter. The standard penicillin was obtained from the United States Department of Agriculture. All titrations of the bone marrow suspensions were accompanied by and compared with this standard.

*Results.*—The results were divided into two groups. In table 1 are listed the results following single injections of penicillin by way of arterial, intravenous and muscular routes. Table 2 includes the data obtained

after two consecutive injections had been given by these same routes. It may be noted that the penicillin levels of the bone marrow varied in different dogs with the same doses, routes and methods of administration, an indication that considerable individual variation existed. The highest peak levels usually occurred ten minutes after an injection.

With single injections, bone marrow levels were higher after intravascular (intravenous or intra-arterial) administration than after intramuscular administration. Definite, consistent differences between the intravenous and the intra-arterial routes could not be demonstrated.

When two injections of 2,000 units per kilogram each were given twenty or thirty minutes apart, a conspicuous elevation in the concentration of the drug in the bone marrow was noted after the second

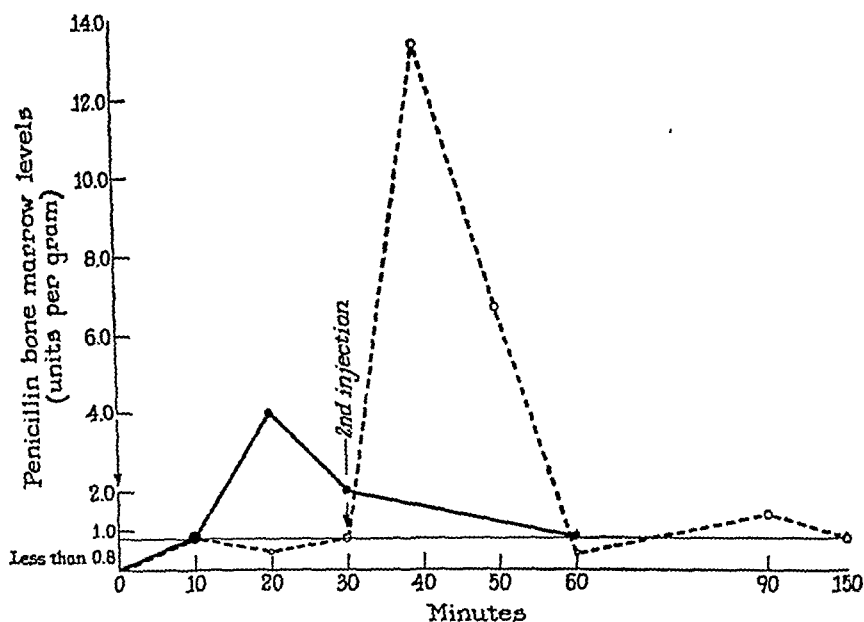


Chart 1 (dog 11).—The solid line indicates the levels of penicillin in the bone marrow after the intravenous administration of 4,000 units per kilogram; the line of dashes, the levels after an injection of 2,000 units per kilogram administered intravenously, followed by an intra-arterial injection of 2,000 units per kilogram of body weight.

injection. This level exceeded by far that found after a single injection of the same total amount of penicillin. The marrow of all dogs which received an intra-arterial dose after a preliminary intravenous injection showed this distinct rise in concentration of the drug. Three of 5 dogs given two consecutive intra-arterial injections also showed considerable elevation in the concentration of penicillin in the marrow. If the two injections were both given by the intravenous route, some elevation of the level of penicillin in the bone marrow was seen, but the rise was not so pronounced as the increases following the other means of administration. Thus, in almost every instance, a noticeable increase in the

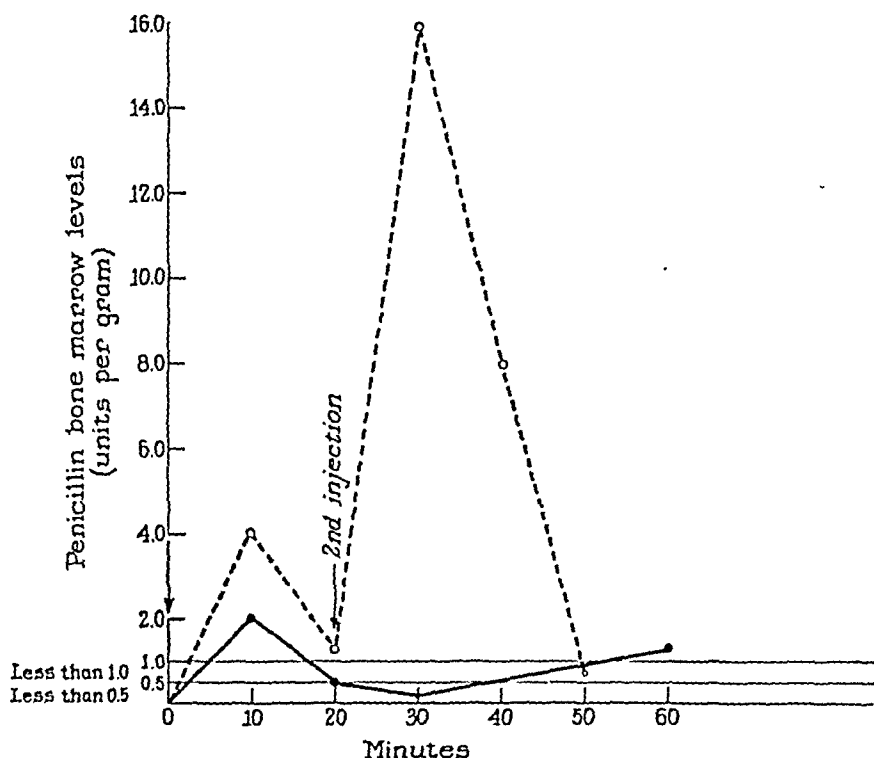


Chart 2 (dog 3).—The solid line indicates the levels of penicillin in the bone marrow after the intra-arterial administration of 2,000 units per kilogram; the line of dashes, the levels after an intravenous injection of 2,000 units per kilogram, followed by an intra-arterial injection of 2,000 units per kilogram of body weight.

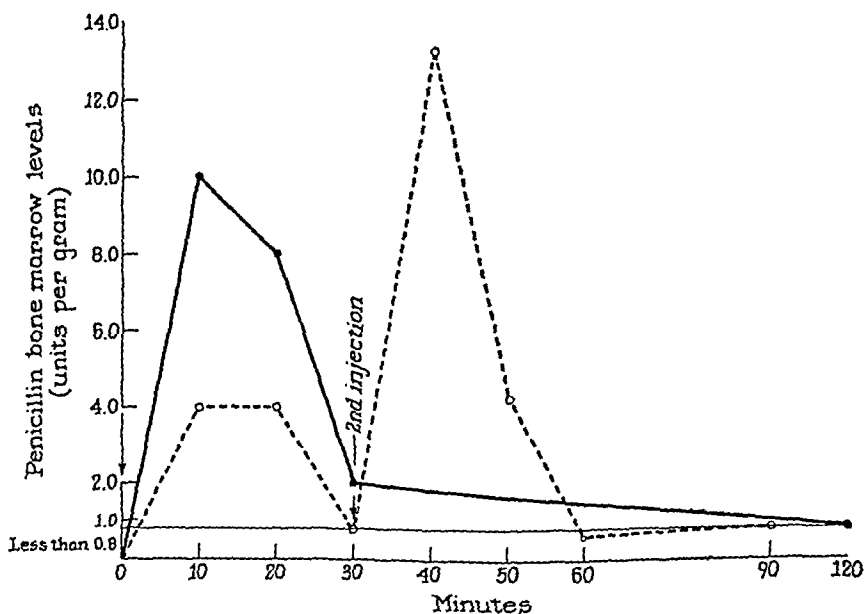


Chart 3 (dog 10).—The solid line indicates the levels of penicillin in the bone marrow after the intravenous administration of 4,000 units per kilogram; the line of dashes, levels after an intra-arterial injection of 2,000 units per kilogram of body weight, followed by another intra-arterial injection of the same amount.

concentration of penicillin in the bone marrow occurred whenever a booster intra-arterial injection was given after a priming intravascular dose. It may also be noted that an intramuscular followed by an intra-arterial injection failed to produce any significant elevation.

After the animals' recovery, the operation was repeated on some dogs, the intact side being used. In this way, comparative observations on different doses, routes and methods of administration could be made in the same dogs. The data are illustrated in charts, 1, 2 and 3. As may be seen from chart 1, a preliminary intravenous injection followed by an intra-arterial injection produced a considerably greater concentration of penicillin in the marrow than did the same total dose administered as a single intravenous injection. Similar elevations resulting from booster arterial injections are illustrated in charts 2 and 3.

Individual variation is best illustrated by a comparison of the results of experiments on dogs 9 and 10. It may be noted that in dog 9, even after two arterial doses, little or no penicillin could be found in the marrow, although an assay of the blood showed a level of 2.0 units per cubic centimeter thirty minutes after the second injection. This animal was one of our older dogs, and it was believed that age and its effect on the vasculature might account for these findings. By comparison, dog 10, also an old animal, showed very satisfactory levels after the two arterial injections. Both dogs weighed about the same and had received approximately the same dose by the same routes and methods; yet their experimental results were completely at variance. Many factors, such as different vascular patterns in the bone and barriers through which the penicillin must penetrate, may account for this apparent discrepancy. Variations in systemic absorption, diffusion and excretion in different animals may also play a part.

Finally, after analyzing our results for any differences in the duration of penicillin levels in the marrow after various routes and methods of administration, we were unable to note any clearcut differences, since considerable variation in this respect also existed.

#### COMMENT

It has been demonstrated that in normal young dogs a decided elevation in the concentration of penicillin in the bone marrow results from a priming intravascular injection of the drug, followed by a booster intra-arterial dose. This level is considerably greater than that obtained after a single injection of the same total amount irrespective of the route of administration. Since the degree of diffusion of an antibiotic substance like penicillin is proportional to its concentration, it is logical to assume that if a higher concentration can be achieved greater diffusion of the drug through the marrow cavity will result. Rather poor results

have been reported with penicillin alone in the treatment of chronic osteomyelitis. Robertson<sup>6</sup> stated that long-standing sepsis involving the bone must be considered an unfavorable field for treatment with penicillin administered either locally or systemically. On the other hand, Key<sup>7</sup> has reported that this agent, in conjunction with the proper surgical treatment, has been found a useful adjunct to therapy. According to Buchman and Blair,<sup>8</sup> who described the pathology of the disease, the unfavorable results may be attributed to the poor blood supply and the avascular contents of the diseased marrow, which is therefore beyond the reach of any therapeutic agent carried by the blood stream. In the light of our experimental findings with booster intra-arterial injections, it is believed that higher penicillin levels in the bone can be obtained by this method than with the others aforementioned, and that greater penetration will be favored thereby. The organisms responsible for chronic osteomyelitis are, as a rule, sensitive to the antibiotic; and if they are reached by a sufficient concentration of the drug, a better therapeutic result should ensue. Gerber, Schwartzman and Baehr<sup>9</sup> demonstrated a greater penetration of penicillin into foci of infection when higher peak levels in the blood were produced. In the same manner, greater diffusion and penetration into a focus of infection inside a bone should result if higher concentrations of the drug in the marrow cavity were achieved. For this reason, and because of our experimental results, it is believed that a clinical trial of the method of booster arterial injection in the treatment of osteomyelitis is justified.

A review of the literature reveals that the limited use of this method is directly attributable to the previous absence of an effective, safe anti-septic agent. At the outbreak of World War I, Heddaus<sup>10</sup> successfully treated 6 patients with tetanus by the intracarotid injection of antitoxin. He stated that Leriche had preceded him in this technic by several months. In the same year (1914) the Fiolles<sup>11</sup> suggested the infusion of oxygenated fluid into the major arteries of the extremities infected

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6. Robertson, I. M.: Penicillin in Bone Infections, *Brit. M. J.* **1**:519-521 (April 15) 1944.

7. Key, J. A.: Penicillin and Sulfonamides in the Treatment of Osteomyelitis and Pyogenic Arthritis, *Bull. New York Acad. Med.* **21**:87-98 (Feb.) 1945.

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11. Fiolle, J., and Fiolle, P.: Essais d'hématose artificielle et d'angéiothérapie artérielle, *Marseille méd.* **51**:597-603 (Sept. 1) 1914.

with the gas bacillus. Later, in this country, Hirsch and associates<sup>12</sup> safely and easily administered intracarotid injections of neoarsphenamine U. S. P. and sulfarsphenamine U. S. P. in the treatment of dementia paralytica. Kolmer<sup>13</sup> described the results of the introduction of various chemicals and serums into the carotid arteries of dogs with experimental pneumococcic and streptococcic meningitis. Later, he reported<sup>14</sup> cases of clinical meningitis in some of which recovery followed the intracarotid administration of serum and in some cases, Pregl's solution<sup>15</sup> and acriflavine. In 1933, Lamas<sup>16</sup> injected merbromin N. F. into the aorta in the treatment of subphrenic abscess. The 82 patients who received arterial injections included 5 with compound fracture, 8 with osteomyelitis and 50 with various abdominal conditions. With the intent of refining the technic of arterial injection, Huet and Bargeton<sup>17</sup> investigated the effects of various concentrations of different solutions on the vessel wall. They concluded that isotonicity is desirable and that the  $p_H$  should lie between 7.0 and 8.3, in order that spasm and organic changes might be avoided. In 1938, Luccarelli<sup>18</sup> published a series of 36 cases of infection of an extremity, with and without gangrene, and 1 case of meningitis, in all of which by the introduction of "salvakra" (a preparation of gentian violet medicinal) into the major artery supplying the part. Although it is difficult to estimate his success from the short case reports, his succinct introduction on the rationale of the method is excellent. In short, the ingenuity displayed in these reports is more impressive than the account of the therapeutic efficiency of the injected substances.

With the development of future antibiotics, the anticipated increase in range of action may possibly be accompanied with a greater toxicity.

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12. Hirsch, H. L.; Myerson, A., and Halloran, R. D.: Intracarotid Route in the Treatment of General Paresis, Boston M. & S. J. **192**:713-717 (April 9) 1925.

13. Kolmer, J. A.: The Intracarotid Treatment for Experimental Pneumococcus Meningitis, Arch. Otolaryng. **9**:509-527 (May) 1929.

14. Kolmer, J. A.: The Intracarotid Method of Treatment for Meningitis with Recoveries, J. A. M. A. **96**:1358-1361 (April 25) 1931.

15. Pregl's solution (concentrated) is a complex aqueous solution containing 3 per cent of available iodine in the form of hypoiodite and hypoiodate ions and some free iodine (Cowan, A., and Cowan, T. H.: Superficial Punctate Keratitis, Arch. Ophth. **19**:709-713 [May] 1938, p. 710).

16. Lamas, A. C.: Therapeutique par voie arterielle, Cong. franç. de chir. **42**:384-398, 1933.

17. Huet, P., and Bargeton, D.: Sur quelques effets des injections intra-arterielles, Presse méd. **44**:677-681 (April 22) 1936.

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In this connection, it may be noted that in 1909 von Oppel<sup>19</sup> compared the effects of injecting cocaine into the aorta and into the inferior vena cava of rabbits. He discovered that a given dose was eight to ten times as toxic in the vein as in the artery and concluded that the larger the capillary bed distal to the site of the injection, the lower the toxicity.

The technic of intra-arterial injection need not be confined to the administration of antibacterial substances. Other physiologically active substances and other antibiotic agents may be utilized in the same manner. As long ago as 1910, Ransohoff<sup>20</sup> induced regional anesthesia by injecting cocaine into peripheral arteries. It is our feeling that the method is fully worthy of more intensive investigation.

#### SUMMARY AND CONCLUSIONS

The rationale of the arterial administration of antiseptic substances is presented.

Levels of penicillin in bone marrow following single intramuscular, intravenous and intra-arterial injections were compared. With reference to these levels, no consistent difference with respect to bone marrow levels could be demonstrated between the intravenous and the intra-arterial route of administration.

An intra-arterial injection following a preliminary intravenous or intra-arterial dose resulted in a concentration of penicillin in the bone marrow far in excess of that obtained by a single injection of the same total dose.

The application of these observations to the treatment of infectious processes in bones is discussed.

Miss B. Toharsky and Miss R. Schapira gave technical assistance.

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19. von Oppel, W. A.: *Experimentelle Grundlagen der arteriellen Anästhesie*, München. med. Wchnschr. **56**:1772-1775 (Aug. 31) 1909.

20. Ransohoff, J. L.: *Terminal Arterial Anaesthesia*, Ann. Surg. **51**:453-456 (April) 1910.

## Editorial

### INTRAVENOUS ADMINISTRATION OF GELATIN AND HISTOLOGIC CHANGES IN THE KIDNEY

ONE OF the major problems in the development of a plasma substitute has been the elimination of toxic properties inherent in the substitute or produced in its processing. A number of proposed plasma substitutes known to increase the plasma volume such as acacia, pectin, globin and bovine albumin have been abandoned only because of these toxic properties.

In the early years of World War II several gelatins were studied extensively as substitutes for plasma. One of these, a preparation designated as Knox P-20, is the subject of a special report from the National Research Council published in 1944 in *The Journal of the American Medical Association*,<sup>1</sup> which stated that a gelatin of the Knox P-20 type is of optimal value in the treatment of hemorrhage and shock. This report also stated that "many repeated injections in animals have been given without evidence, histologic or clinical, of toxicity or irreversible accumulation."

Knox P-20 gelatin is prepared from the hard bones of cattle and differs in that respect from other gelatins prepared from skins and hides. It is prepared especially for intravenous use in a plant apart from the commercial manufacture of gelatin. Through the combination of its source material and its processing, Knox P-20 is a unique colloid for intravenous use in that it is nontoxic and an adequate replacement for lost plasma volume.

Attention has been directed by several investigators to the differences in gelatins derived from bone and from hides.<sup>2</sup> The ossein gelatin, Knox P-20, is a poorly degraded gelatin which has a predominantly long chain molecular structure which permits relatively slow excretion by the kidney. The gelatin prepared from hides for intravenous use is

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1. Evaluation of Studies on Gelatin Preparations for Intravenous Use, National Research Council, J. A. M. A. **125**:284 (May 27) 1944.

2. Koop, C. E.: The Use of Specially Prepared Gelatin Solution as a Plasma Substitute, S. Clin. North America **24**:1300-1315 (Dec.) 1944. Memoranda and Reports on Physical Chemical Properties of Gelatin and Other Blood Substitutes, OEMcmr Contracts 139 and 142.



a highly degraded colloid of short chain molecular structure allowing rapid excretion of the gelatin by the kidney.

The short chain gelatins may be excreted in as short a period as twelve hours, while the unmetabolized portion of Knox P-20 may remain in the circulation because of its slower excretion by the kidney for periods up to five days.<sup>3</sup>

The recent publication by Skinsnes<sup>4</sup> relative to the production of nephrosis by a hide gelatin prompted us to review our own histologic material relative to the infusion of Knox P-20 and possible renal damage. We have reported previously a summary of our findings in the dog and in man. Renal function, as determined by urea clearance, was apparently unimpaired after single and repeated infusions of gelatin.<sup>3a</sup>

No evidence of chronic renal damage or of the storage of gelatin was noted in normal dogs given single and repeated gelatin infusions.<sup>3</sup> This impression was confirmed in the study of human autopsy material.<sup>3a</sup> A review of our own histologic material has not altered these conclusions.

Our investigations have shown that Knox P-20 and other gelatins are not associated with histologic changes in the kidney, with changes in renal function or with deleterious reactions even in those with a diminished renal reserve. Lowell and her co-workers<sup>6</sup> found no significant change in urine urea nitrogen in 20 dogs, although there was transient albuminuria for twenty-four hours. "Other tests pertaining to cardiac, hepatic and renal function showed no changes." The only constant finding in histologic studies of the kidneys of mice, rabbits and dogs after infusion with fifteen varieties of bone gelatin was an

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3. (a) Koop, C. E.; Fletcher, A. G.; Riegel, C., and Lockwood, J. S.: Gelatin as a Plasma Substitute: A Preliminary Report of Clinical Experience, *Surgery* **15**:839-858 (May) 1944. (b) Koop, C. E.; Riegel, C.; Grigger, R. P., and Barnes, M. T.: A Study of Protein Hydrolysates, Ossein Solution and Glucose in Parenteral Nutrition, *Surg., Gynec. & Obst.* **84**:1065-1070 (June) 1947.

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6. Lowell, A.; Colcher, H.; Kendall, F. E.; Patek, A. J., Jr., and Seegal, D.: A Comparison of the Effects of High and Low Viscosity Gelatins After Their Intravenous Injection in Man, *J. Clin. Investigation* **25**:226-236 (March) 1946.

eosinophilic precipitation in Bowman's space when the tissues were fixed with Zenker's solution.

Jacobson and Smyth<sup>7</sup> found no change in urea clearance in 5 patients after infusion of a bone gelatin. Popper's group<sup>8</sup> found no histologic changes in kidneys in seven autopsies after infusion of gelatin in man. Morehead and Little<sup>9</sup> found an inflammatory lesion present in the kidney in more than one half of 9 dogs which received infusions of a bone gelatin. This lesion represented to them the interstitial nephritis commonly seen in dogs and described by Bloom.<sup>10</sup>

Oliver,<sup>11</sup> using a microdissection technic, revealed no instance of frank evidence of tubular epithelial damage such as necrosis of the cells. Administration of gelatin caused only a transient loculation in the proximal convoluted tubules in the kidney. Chemical identification of these droplets was not possible; however, one can assume that they were due to reabsorbed gelatin which attracted water and caused the hydropic swelling which morphologically simulates that produced by sucrose.<sup>11a</sup>

The renal histologic sections described by Skinsnes<sup>4</sup> can only mean that some substance is being vigorously reabsorbed or excreted by the proximal tubule cells. Oliver<sup>11</sup> has shown that the concept of "hydropic degeneration" simply means that eosinophilic granular material (e. g., albumin) appearing in the glomerular filtrate is being reabsorbed by the proximal tubular cells. Since it is now known that a certain amount of albumin with diameters of 150 by 38 angstrom units normally passes through the glomerular membrane,<sup>12</sup> gelatin with a

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7. Jacobson, S. D., and Smyth, C. J.: Gelatin as a Substitute for Plasma: Observations on Its Administration to Human Beings, *Arch. Int. Med.* **74**:254-257 (Oct.) 1944.

8. Popper, H.; Volk, B. W.; Meyer, K.; Kozoll, D. D., and Steigmann, F.: Evaluation of Gelatin and Pectin Solutions as Substitutes for Plasma in the Treatment of Shock, *Arch. Surg.* **50**:34-45 (Jan.) 1945.

9. Morehead, R. P., and Little, J. M.: A Morphological Study Following the Intravenous Administration of Gelatin Solutions to Dogs, *Am. J. Path.* **21**:333-338 (March) 1945.

10. Bloom, F.: Classification and Pathology of Renal Disease in Dog: Comparison with Nephritis in Man, *Arch. Path.* **28**:236-245 (Aug.) 1939.

11. Oliver, J., in a report to the National Research Council, Division of Medical Sciences, Committee on Blood Substitutes, September 1943.

11a. Anderson, W. A. D., and Bethea, W. R., Jr.: Renal Lesions Following Administration of Hypertonic Solutions of Sucrose: Report of Six Cases, *J. A. M. A.* **114**:1983-1987 (May 18) 1940.

12. Oliver, J.: New Directions in Renal Morphology: A Method, Its Results and Its Future, in *Harvey Lectures, 1944-1945*, Baltimore, Williams & Wilkins Company, 1946, pp. 102-155. Smetana, H.: The Permeability of the Renal Glomeruli of Several Mammalian Species to Labelled Proteins, *Am. J. Path.*

smaller diameter of 18 angstrom units will be found in the glomerular filtrate. Thus Skinsnes' sections may represent the proximal tubule reabsorption of gelatin, especially since it can be demonstrated in the plasma seven to twelve days after its administration.

The absence of cellular degeneration as indicated by lack of necrosis in the proximal tubules or of degeneration of the brush border would indicate that marked tubular damage did not occur, especially since gelatin was probably present in the plasma of the patients at death.

The routine clinical studies of renal function and urea clearance, phenolsulfonphthalein and concentration tests are qualitative. In a recent study of the nephrotoxicity of an antibiotic, 20 to 80 per cent reduction in renal plasma flow, glomerular filtration rate, maximal tubular excretion of *p*-aminohippurate and maximal tubular reabsorption of phosphate occurred, while there were no statistically significant alterations in blood urea nitrogen or phenolsulfonphthalein and urea clearance.<sup>13</sup>

Since the qualitative tests of renal function are not sensitive enough to pick up even major aberrations in renal function and since casts appear in the urine only intermittently and are easily overlooked quantitative renal function tests should be performed completely to rule out nephrotoxicity.

A program to test the quantitative renal function following infusion of gelatin is now under way in this laboratory.

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23:255-267 (March) 1946. Terry, R.; Hawkins, D. R.; Church, E. H., and Whipple, G. H.: Proteinuria Related to Hyperproteinemia in Dogs Following Plasma Given Parenterally: A Renal Threshold for Plasma Proteins, *J. Exper. Med.* 87:561-573 (June) 1948.

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# SURGICAL IMPLICATIONS OF ACUTE PANCREATITIS

An Analysis of Eighty-Five Cases

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THE RECOGNITION of increased blood diastase values in instances of acute pancreatitis by Elman<sup>1</sup> and the subsequent development of a simple, rapid and accurate method of determining the diastatic activity of both blood and urine by Somogyi<sup>2</sup> have led to the more frequent recognition of mild or transient forms of this disease.

A decade ago this subject was reviewed, and case reports of 21 patients with acute pancreatitis seen at St. Louis Jewish Hospital and St. Louis City Hospital were presented in a paper from these laboratories.<sup>3</sup> From 1934, when the Somogyi diastase methods were first used, until July 1947 there have been 65 patients with acute pancreatitis seen at the St. Louis Jewish Hospital. The history of these patients subsequent to their attacks of pancreatitis is available in most instances. As the cases accumulated, characteristics of the disease which we did not previously appreciate have become more apparent and the place of surgical procedures has become more clearly defined.

## INCIDENCE

The incidence of acute pancreatitis is much greater than is usually recognized. Thus, during the period in which 65 patients with acute pancreatitis were seen, 51,500 patients were admitted to the surgical

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1. Elman, R.; Arneson, N., and Graham, E.: Value of Blood Amylase Estimations in the Diagnosis of Pancreatic Disease, *Arch. Surg.* **19**:943 (Dec.) 1929.

2. Somogyi, M.: Micromethods for the Estimation of Diastase, *J. Biol. Chem.* **125**:399, 1938.

3. Gray, S. H.; Probstein, J. G., and Heifetz, C. J.: Transient Acute Pancreatitis, *Ann. Surg.* **108**:1029, 1938.

and medical services of the hospital. Some of them were admitted with acute pancreatitis on several occasions, and 1 patient had two attacks during the same period in the hospital. Of these 51,500 patients, 84 were admitted for acute pancreatitis. Hence, about 1 out of 600 patients admitted to the surgical and medical services had acute pancreatitis. The true incidence in this hospital is probably even greater, because in the first years of this series many cases were undoubtedly overlooked.

This figure is to be contrasted with that reported by Fallis and Plain<sup>4</sup> in 1939. They reported an incidence of 1 case of pancreatitis in every 10,000 persons admitted when the diagnosis of pancreatitis was based on the findings at operation and preoperative diagnostic determinations of the blood diastase were not performed. It is readily apparent what valuable diagnostic adjuncts determinations of blood and urine diastase are and how easy it is to overlook mild transient forms of acute pancreatitis. In this hospital it has become routine to order a determination of the blood diastase in any case in which pain in the upper abdominal area is presented.

#### ASSOCIATION WITH DISEASE OF THE GALLBLADDER

The association of acute pancreatitis with disease of the gallbladder is so well known as to be hardly worth repeating. Some aspects of this relationship have not been sufficiently stressed.

There is a significant number of patients with acute pancreatitis who have a coincident acute cholecystitis. McWhorter<sup>5</sup> reported that 22 per cent of patients with acute pancreatitis had acute cholecystitis. Fallis and Plain,<sup>4</sup> on the basis of operative findings, found the incidence to be 15.4 per cent. Lewison<sup>6</sup> reported an incidence of 3 per cent. McCorkle<sup>7</sup> reported that 22 per cent of patients with acute pancreatitis had a coincident acute cholecystitis.

A review of the physical findings leads us to suspect concurrent acute cholecystitis on clinical grounds in 16 of 85 episodes of pancreatitis. Actually, 15 episodes of pancreatitis occurred after cholecystectomy. Hence 16 of a possible 70 patients presumably had concurrent acute cholecystitis, an incidence of 23 per cent. However, we are unable to state with certainty how many of our patients with acute pancreatitis had concurrent acute cholecystitis, because early operation is not the accepted practice in this hospital in cases of acute cholecystitis or acute pancreatitis.

4. Fallis, L. S., and Plain, G.: *Acute Pancreatitis*, *Surgery* **5**:358, 1939.

5. McWhorter, G. L.: *Acute Pancreatitis*, *Arch. Surg.* **25**:958 (Nov.) 1932.

6. Lewison, E. F.: *Acute Pancreatitis*, *Arch. Surg.* **41**:1008 (Oct.) 1940.

7. McCorkle, J., and Goldman, L.: *The Clinical Significance of the Serum Amylase Test in the Diagnosis of Acute Pancreatitis*, *Surg., Gynec. & Obst.* **74**:439, 1942.

During the period in which these patients were seen, 121 patients with acute cholecystitis, inclusive of the 16 mentioned previously, were seen. Thus, 13 per cent of the patients with acute cholecystitis had concurrent pancreatitis. McCorkle and Goldman<sup>7</sup> found that 14 of 42 patients with cholecystitis had concurrent pancreatitis.

This significant correlation between acute pancreatitis and acute cholecystitis has three possible explanations:

1. The acute cholecystitis causes the acute pancreatitis.
2. The acute pancreatitis causes the acute cholecystitis.
3. Both the acute pancreatitis and the acute cholecystitis are caused by a third factor common to both.

The first explanation can hardly hold in all cases, because acute pancreatitis occurs not uncommonly in persons whose gallbladder has been previously removed. As stated before, fifteen of the attacks of pancreatitis in our series occurred in 11 persons whose gallbladders had been removed.

It is not readily apparent how acute pancreatitis could cause acute cholecystitis.

The third explanation, that the relationship between acute cholecystitis and acute pancreatitis is due to a common etiologic factor, seems more tenable. The common factor would seem to be obstruction distal to the junction of the pancreatic and common bile ducts converting them into a "common channel." Thus Bisgard and Baker<sup>8</sup> were able to produce concurrent acute pancreatitis and acute cholecystitis experimentally by obstructing the common duct of goats distal to the entrance of the pancreatic duct.

That there actually is a reflux of pancreatic juice into the gallbladder during an acute attack of pancreatitis was shown in 1933 by Popper,<sup>9</sup> who found increased amounts of diastase in the gallbladder bile in 15 of 16 patients with acute pancreatitis. Since the gallbladder bile does not normally contain diastase,<sup>10</sup> the diastase must have gotten into the gallbladder by reflux through a common channel. These observations, which can only be explained by the "common channel" theory of pancreatitis, have been confirmed by us in 2 patients with acute pancreatitis operated on at this hospital since the series was collected. One case is presented here in detail:

8. Bisgard, J. D., and Baker, C. P.: Studies Relating to Pathogenesis of Cholecystitis, Cholelithiasis and Acute Pancreatitis, *Ann. Surg.* **112**:1006, 1940.

9. Popper, H. L.: Pankreassaft in den Gallenwegen: Seine pathogenetische Bedeutung für die Entstehung der akuten Pankreaserkrankungen, *Arch. f. klin. Chir.* **175**:660, 1933.

10. Gray, S. H.; Probst, J. G., and Heifetz, C. J.: Clinical Studies on Blood Diastase, *Arch. Int. Med.* **67**:805 (April) 1941.

D. B., a 59 year old woman, entered the hospital on July 11, 1947, with a history of attacks of sharp epigastric pain occurring during the preceding three years. These pains had become more frequent during the preceding three weeks; they started in the mid-epigastrium and radiated to the flanks. The pain had always been associated with nausea. During the past year the patient had lost 12 pounds (5.4 Kg.).

On her admission to the hospital the blood diastase was 59 units; the white blood cell count was 5,000. The temperature, pulse and respirations were normal. There was epigastric tenderness. Two days after her admission the patient suddenly had severe epigastric pain, more severe than any she had experienced in the past. Glyceryl trinitrate failed to relieve it. Administration of pantopon® (a mixture of the hydrochlorides of the opium alkaloids)  $\frac{1}{2}$  grain (0.02 Gm.) gave considerable relief. The blood diastase level on that day was 1,580 units. The pain persisted during the next day. There was diffuse muscle guard and tenderness over the entire abdomen, but it was most marked in the upper region and particularly in the right upper quadrant. There was a questionable mass in the right upper quadrant, but the muscle guard prevented adequate palpation.

On the second day of this acute episode the diastase level was 1,900 units. The white blood cell count had risen to 26,000. Bile and urobilinogen (3 plus) were present in the urine. The icterus index was 30. The reaction to the van den Bergh indirect test was positive. On the night of the second day the abdomen was explored. It contained yellowish-tinged free fluid. The liver was enlarged and the edge rounded. The gallbladder was fiery red and extremely thin. The pancreas was enlarged, and the serosa over it was edematous.

The gallbladder was aspirated and the contents sent to the laboratory for culture and for determination of the diastase and nitrogen content. A biopsy of material from the pancreas was made. A cholecystostomy was then performed. The blood diastase level was obtained at the time of operation.

The postoperative convalescence was uneventful. The pancreatic biopsy showed the characteristic findings of "acute interstitial pancreatitis." The gallbladder bile, which normally contains no diastase, contained 1,095 units. Its nitrogen content was 1.17 per cent. The blood diastase level, obtained simultaneously, was 430 units. Culture of the contents of the gallbladder revealed *Bacillus coli*.

The obvious explanation of the finding of diastase in the gallbladder is that there was a reflux of pancreatic juice into the gallbladder. An alternate explanation might be advanced. It might be argued that the presence of diastase was due to transudation from the gallbladder wall as part of the process of inflammation. That this explanation does not hold is shown by the finding of a higher concentration of diastase in the gallbladder bile than in the blood. Furthermore, it cannot be said that the inflammatory exudate was concentrated in the gallbladder by absorption of water, thus accounting for the higher diastase level, because the protein content of the material in the gallbladder was less than that of the blood plasma.

Popper also found that the diastase content of gallbladder bile was higher than that of the blood during acute pancreatitis.<sup>9</sup>

#### CLINICAL FEATURES OF ACUTE ATTACKS

An analysis of the physical findings in our series fails to reveal any constant distinctive pattern which would enable the diagnosis to be made with certainty without exploration or determination of serum or urine

diastase levels. The pain is usually epigastric. It may radiate to the right or to the left, to the back or to the shoulders. Often it was "cramping" or "colicky" in character. The severity varied, but morphine was usually required for relief. About half of the patients vomited, and most of the remainder were nauseated. Prostration is the rule, and the patients take to bed voluntarily. Epigastric tenderness is an almost constant finding. In addition, there may be tenderness in the left or right upper quadrant. In some cases there is generalized abdominal tenderness. Muscle guard is variable. Cases presenting tenderness in the right upper quadrant and muscle guard are indistinguishable from cases of acute cholecystitis. Indeed, there may actually be a concomitant acute cholecystitis. At times an ill defined, tender mass may be felt in the right upper quadrant. In 1 case this proved to be liver rather than gallbladder at operation, although the gallbladder was inflamed. The temperature is elevated only moderately. In some cases the elevation is slight.

The white blood cell count is increased but not markedly, and counts of over 18,000 are not common. Counts of 8,000 to 11,000 are not unusual. The icterus index is usually increased.

The distinctive laboratory finding is an increased blood and urinary diastase level. The significance of determinations of blood and urine diastase has been previously reviewed by Elman,<sup>11</sup> Gray, Probstein and Heifetz<sup>3</sup> and Lewison<sup>6</sup> among others.

#### PROGNOSIS

The immediate prognosis after an attack of pancreatitis in our series was good. There were 3 deaths in the eighty-five attacks of pancreatitis. Two deaths occurred on the second day of the disease, while the third death occurred on the twenty-fourth day.

There is, however, a great tendency for the disease to recur. Its recurrent nature has been mentioned by a number of authors. Love<sup>12</sup> in 1926 emphasized that in 31 of the 51 cases he reported there was a history of previous attacks. Elman<sup>11</sup> also emphasized the recurrent nature of the disease. He reported 38 cases of transient pancreatitis, 4 of his own and 34 from the literature; in 24 there had been previous attacks. Fallis and Plain<sup>4</sup> noted that 53.8 per cent of their 26 patients had similar pain in the past. Lewison<sup>6</sup> reported 71 per cent of his 35 patients had a history of previous attacks.

These previous attacks for the most part have been considered to be pancreatitis because of their similarity to an attack which was posi-

11. Elman, R.: Acute Interstitial Pancreatitis, Surg., Gynec. & Obst. **57**: 291, 1933.

12. Love, R. J.: Acute Pancreatitis, Lancet **2**:1262, 1926.



tively diagnosed either by exploration or by the finding of high blood diastase values. The validity of a diagnosis of previous attacks on such a basis is always open to question in the absence of operative findings or of a high blood diastase level. Occasionally when patients are questioned closely, they will state that the "similar attacks" in the past were not really as severe as the one during which the diastase level was increased. There is a possibility, therefore, that some of these "previous attacks" based on history were really not pancreatitis.

Nevertheless, of our 65 patients with pancreatitis, 14 have been observed during recurrent attacks of pancreatitis, verified by the finding of a high blood diastase level. Another 15 patients gave a history of one or more similar attacks in the past.

Because of the questionable character of a diagnosis of pancreatitis based on history alone, we have confined our further analysis of these recurrent cases to those in which increased blood or urine diastase levels were actually found on several occasions.

The interval between these attacks is given in the table. Before,

*Interval Between Attacks*

Patient	First and Second Attack, Mo.	Second and Third Attack, Mo.
R. G.....	3½	6½
M. E.....	1	
C. E.....	12	
M. F.....	11½	
C. C.....	6	
E. K.....	1½	
T. C.....	3½	
S. C.....	30	
I. K.....	32	4
B. S.....	¼	
R. S.....	4	2
I. L.....	42	
G. F.....	2	

after or between "verified" attacks of pancreatitis the patient may have epigastric pains during which the blood diastase is normal. The pathogenesis of these pains is not known. It is possible that these attacks may be pancreatitis but that the rise in the diastase level was too evanescent to be discovered.

The sequelae of these episodes of acute transient pancreatitis have been of particular interest to us since the recent description of "chronic relapsing pancreatitis" by Comfort and his co-workers.<sup>13</sup> These authors described cases of steatorrhea, diabetes and pancreatic calculi following

13. Comfort, M. W.; Gambill, E. E., and Baggenstoss, A. H.: Chronic Relapsing Pancreatitis, *Gastroenterology* 6:239, 1946.

recurrent abdominal pain. The episodes of abdominal pain described frequently did not correspond to what we have considered to be the typical clinical picture of acute transient pancreatitis. Reports of the blood diastase level during the acute attacks were lacking in most cases, and in some it was normal. As we have previously stated, a diagnosis of acute pancreatitis of the "edematous" or "hemorrhagic" type is questionable without the finding of an increased blood diastase level at least during the beginning of the attack. Comfort, Gambell and Baggenstoss have suggested that the interstitial fibrosis and atrophy of the parenchyma, which pathologically characterizes "chronic relapsing pancreatitis," may be due to repeated attacks of acute interstitial inflammation of the pancreas. It is therefore of considerable interest to find that the clinical evidences of chronic pancreatitis described by these authors have not been found in the follow-up of our series of cases of acute pancreatitis. We are now reviewing our cases of chronic pancreatitis diagnosed histologically at operation or at autopsy.

#### TREATMENT

Since 1934 it has been the generally accepted policy of surgeons at this hospital not to operate during the acute episode of pancreatitis, no distinction being made between hemorrhagic and interstitial pancreatitis. On two occasions this policy was disregarded and the patients were operated on after a diagnosis of pancreatitis was made. In 1 case acute hemorrhagic pancreatitis was found. The patient died on the day of operation. The other patient recovered uneventfully.

The other 83 patients with attacks of pancreatitis were treated conservatively. There were 2 deaths in this group. One patient, aged 75, died on the second day of her disease. Autopsy was not permitted. The other fatality occurred twenty-four days after the onset of the acute pancreatitis. At autopsy an abscess in the head of the pancreas and multiple abscesses of the liver were found.

Although surgical intervention is not indicated in the treatment of the acute attack, exploration does seem to be warranted when inflammatory signs and symptoms persist. Then the operative procedure is really directed at the complications of acute pancreatitis rather than at the pancreatitis itself. It might have been possible to avoid one of the fatalities in this series had this rule been followed. Since this series was collected we have observed 1 case which illustrates the place of "delayed surgery" in the treatment of acute pancreatitis.

C. B., a 79 year old woman, was admitted to the Jewish Hospital on Sept. 11, 1947. Four weeks earlier, while in Frankfort, Mich., she had an attack of severe abdominal pain, colicky in nature, accompanied with fever. She was given sulfonamide compounds and then penicillin. However, she continued to have

constant nausea, indigestion and epigastric discomfort. She had a temperature of up to 102 F. daily.

Examination at the time of her admission to this hospital revealed a fairly alert elderly woman. She had a systolic murmur at the apex. The liver was felt extending 4 fingerbreadths below the costal margin. There was a sense of resistance in the epigastrium imparted to the palpating hand, but no mass was felt.

A series of roentgenograms showed a nonfunctioning gallbladder. No calculi were seen. A gastrointestinal series was interpreted as showing "an extrinsic mass lying in the midline and exerting pressure on the distal end of the stomach without displacing the duodenum." The white blood cell count was 12,400, with a left shift in the differential count. The blood nonprotein nitrogen was 33 and the serum diastase less than 20 units.

On September 17 the upper region of the abdomen was explored through a transverse abdominal incision. The transverse colon and the stomach were fixed to a mass in the head of the pancreas. The gallbladder contained stones. The pancreatic mass was broken into through the transverse mesocolon. A small amount of purulent material was obtained, and then a large piece of necrotic material was removed with a sponge forceps. The cavity left by the removal of this material was drained with a cigaret drain brought out through the wound. The abdomen was closed in layers about the drain. Culture of the abscess revealed *B. coli*. Postoperatively the patient was given penicillin and streptomycin. She was out of bed on the second postoperative day. Her convalescence has been uneventful.

After the attack of acute pancreatitis has subsided the question of cholecystectomy frequently arises, particularly if the Graham test reveals gallstones or a nonfunctioning gallbladder. Fifty-six persons in this series had not undergone an operation on the biliary tract before being observed in an attack of acute pancreatitis. Twelve of these patients subsequently were subjected to operation. All of them underwent cholecystectomy and 6, in addition, explorations of the common duct. In 2 cases stones were found in the common duct. Two of the 12 patients in whom operations on the biliary tract had been performed subsequently were hospitalized for recurrence of pancreatitis. The first patient had recurrences of pancreatitis seven and twelve months after her gallbladder had been removed and her common duct explored. No stones had been found in the common duct. The second patient had her gallbladder removed and three stones removed from the common duct. After a few months she began to have frequent epigastric pains, but not until five years later did she have an attack of pancreatitis verified by a high blood diastase level. Two months later she had another attack of acute pancreatitis with an increase in the blood diastase. Her common duct was reexplored and found to be free of stones. She continued to have the vague epigastric pains which followed her original surgical procedure. These pains occurred even though the T tube, which was placed in her common duct, was left open.

In addition to the 2 patients described who had recurrent acute pancreatitis after cholecystectomy, there were 9 other patients who had acute pancreatitis after undergoing cholecystectomy. Whether these attacks represent recurrences or first attacks is not known.

It is clear that cholecystectomy, with or without exploration of the common duct, in our experience has not been a certain means of preventing acute pancreatitis. Hence, in regard to the decision whether cholecystectomy is indicated after an attack of acute pancreatitis, it appears that if one would have advised cholecystectomy had pancreatitis not developed then one should, of course, continue to advise cholecystectomy. On the other hand, if the history and the roentgenologic findings are such that one would not have advised cholecystectomy had acute pancreatitis not ensued, then one should continue to advise against removal of the gallbladder.

When cholecystectomy is performed after an attack of acute pancreatitis, we believe that the common duct should be explored. In two of the six common ducts that were explored after attacks of acute pancreatitis stones were found. Moreover, should the pancreatitis recur after the surgical procedure, as seems to happen not uncommonly, the question arises of whether a stone in the common duct has been overlooked. It is some comfort to the surgeon to know that he had previously explored the common duct.

It is in the handling of cases in which pancreatitis has developed after cholecystectomy that the most difficult problems arise. The question then is whether to explore or reexplore the common duct.

Of our 11 patients who had acute pancreatitis after a cholecystectomy, in only 1 was reexploration carried out. Nothing was found in or about the common duct to account for the pancreatitis. Of the 10 who were treated expectantly, 5 had proved multiple attacks, but eventually all became free of abdominal pain without surgical intervention.

During July 1947 there had been another patient, not included in this series, who had acute pancreatitis nine years after a cholecystectomy. Her common duct was explored after subsidence of the pancreatitis. Nothing was found.

Our experience would indicate that the occurrence of acute pancreatitis subsequent to a cholecystectomy is not an indication in itself for exploration or reexploration of the common duct.

#### SUMMARY

Acute pancreatitis is not an uncommon disease, but it will be frequently overlooked if determinations of blood or urine diastase are not made in all cases of pain in the upper abdominal area. Frequently there is a coincident acute cholecystitis. The existence of a "common channel"

formed by the pancreatic and common bile ducts seems to be an etiologic factor common to the acute pancreatitis and coincident acute cholecystitis. The finding of a reflux of pancreatic juice into the gallbladder during an attack of acute pancreatitis has been confirmed. Acute pancreatitis, as a rule, subsides spontaneously but tends to recur in about half of the cases. Cholecystectomy, with or without exploration of the common duct, does not prevent the recurrence or onset of acute pancreatitis. The development of acute pancreatitis after a cholecystectomy is not an indication for exploration or reexploration of the common duct. In our experience recurrent pancreatitis has tended to be a self-limited disease. We have had no case in which it progressed to chronic pancreatitis.

## EFFECT OF GASTRECTOMY AND DIVERSION OF DUODENAL SECRETIONS INTO THE TERMINAL PORTION OF THE ILEUM ON DEVELOPMENT OF ULCER

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THE FAILURE of bilateral supradiaphragmatic vagotomy to protect against the development of ulcer in the Mann-Williamson dog, as recently reported,<sup>1</sup> has been the stimulus for the work herein described. This investigation was conducted to determine (1) the effect of total gastrectomy with diversion of the duodenal secretions into the terminal portion of the ileum on the development of ulcer and (2) to determine the possible existence of another factor besides the role of acid in the formation of ulcer in man.

The role of acid in the production of ulcer appears to be too definite<sup>2</sup> to be disputed, and it is also well known that vagotomy produces in the dog a definite decrease in the amount of acid and in the total volume of gastric secretion.<sup>3</sup> However, the failure of vagotomy to protect against the development of ulcer in the Mann-Williamson dog led my colleagues and me to believe that the acid might not be the sole cause of ulcer. The possibility of the presence of another factor of great importance, which might be contained in bile or in pancreatic or duodenal secretion or in all three, exists, since in the Mann-Williamson operation<sup>4</sup> all three secretions are diverted from their usual location just distal to the stomach where experimental ulcers are located, into the terminal portion of the ileum 15 cm. from the ileocecal junction. The beneficial effects on patients with ulcers to whom are administered extracts of the duodenum and upper part of the jejunum, as reported by Ivy<sup>5</sup> and his

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1. Oliver, J. V.: Effect of Vagotomy on Development of the Mann-Williamson Ulcer in the Dog, *Arch. Surg.* **55**:180, (Aug.) 1947.

2. Matthews, W. B., and Dragstedt, L. R.: The Etiology of Gastric and Duodenal Ulcers, *Surg., Gynec. & Obst.* **55**:265, 1932.

3. Hartzell, J. B.: The Effect of Section of the Vagus Nerves on Gastric Acidity, *Am. J. Physiol.* **91**:161, 1929.

4. Mann, F. S., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, *Ann. Surg.* **77**:409, 1923.

5. Ivy, A. C.: The Prevention of Recurrence of Peptic Ulcer: An Experimental Study, *Gastroenterology* **3**:443, 1944.

associates, offer proof that the correction of other possible factors exclusive of the hyperacid one may relieve ulcer in man.

The Mann-Williamson operation for internal duodenal drainage shunts the three secretions into the terminal portion of the ileum approximately 15 to 25 cm. from the ileocecal junction, depriving the experimental animal of their action at the site intended for their full physiologic effect. The loss of these three important secretions explains the ulcers which develop in practically 100 per cent of all experimental animals on which the Mann-Williamson operation is performed.

The question arises of whether the stomal ulcer is due to the action of the gastric juices on the susceptible jejunal mucosa or to the lack of alkaline buffering biliary and pancreatic and duodenal secretions or the physiologic loss of some other important factor found in one or all of the three secretions.

Connell<sup>6</sup> performed a fundusectomy, removing an inverted V-shaped wedge comprising the middle two quarters from the greater curvature of the dog's stomach. The animals were kept under observation for a period of three months, after which they were killed and the following observations made:

1. Gastric motor emptying time was not changed after eight weeks.
2. The size and shape of the stomachs returned to normal after six weeks, with gastric capacity restored to preoperative volume.
3. Within three months gastric acid levels were back to normal and equal to preoperative levels.
4. Histologically, no increase in the number of parietal cells was noted to explain the return of the secretory levels to normal.

Ivy and Fauley<sup>7</sup> performed a fundusectomy, as described, in a series of 13 dogs on whom they had performed a Mann-Williamson operation and fed them a diet of ground raw liver, ground raw pancreas, prepared dog food (pard®) and milk. Seven lived one year, and the remaining 6 lived two years in good nutritional state. At necropsy it was noted that in none of the 13 experimental animals did stomal or jejunal ulcers develop. A return to normal of the gastric acid values was also noted. In a second group of 11 fundusectomized Mann-Williamson dogs fed a stock diet, the average survival time was ten weeks and stomal ulcers were found in 3 of the 11. At necropsy it was observed that the gastric remnant had hypertrophied to approximately the preoperative normal size and the gastric acid values had returned to normal.

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6. Connell, F. G.: Fundusectomy: Experimental, Surg., Gynec. & Obst. **53**:750, 1931.

7. Fauley, G. B., and Ivy, A. C.: The Prevention of Postoperative Jejunal Ulcers, Surg., Gynec. & Obst. **63**:717, 1936.

They concluded that fundusectomy has a prophylactic value in preventing ulcer in the Mann-Williamson dog fed a stock diet and that the special diet prevented the development of the Mann-Williamson ulcer in a fundusectomized animal.

The value of a special diet in delaying the onset of the Mann-Williamson ulcer is to a great extent due to the maintenance of a high degree of nutritional state, but eventually ulcers are inevitable, and if the experimental animal survives long enough a stomal ulcer will develop.

Mann<sup>8</sup> stated that after fundusectomy there is a decrease in the degree of gastric acidity roughly parallel to the amount of stomach removed. There is, however, a return to normal in a few months. No one has been able to determine if the quantity of acid is permanently changed by fundusectomy. In their series of 12 dogs which survived a subtotal gastrectomy with removal of 66 per cent of the stomach for three months or more, jejunal ulcer developed in 7. Hypertrophy and dilatation of the gastric remnant occurred in 6 of the 12 animals. Gastric acidity after three to six months approximated the values for the controls. Gastric motor emptying time, however, was reduced from four and a half to two and a quarter hours.

The effects produced by drainage of the duodenal, biliary and pancreatic secretions back into the stomach following an end to end gastrojejunostomy with closure of the proximal duodenal limb and suturing of the terminal duodenum end to side into the stomach were studied by McCann,<sup>9</sup> who noted the development of jejunal ulcer in 80 per cent of 26 dogs in from one to three months. The ulcers were single, 6 to 10 mm. in diameter, and situated beyond the suture line, and they resembled the human peptic ulcer. In spite of the alkaline buffering effect of the duodenal secretions and the presence of a possible antiulcer factor in these secretions, a stomal ulcer developed which could be explained only on the basis of an increased susceptibility of the jejunal mucosa or the prolonged secretion of a highly acid gastric juice due to liberation of histamine following operation.

Fauley and Ivy,<sup>10</sup> in a series of Mann-Williamson dogs, delayed the onset of the development of ulcer by administration of an alkaline phosphate gel.

8. Mann, F. C., cited by Connell.<sup>6</sup>

9. McCann, J. C.: Experimental Peptic Ulcer, *Arch. Surg.* **19**:600 (Oct.) 1929.

10. Fauley, G. B., and Ivy, A. C.: An Attempt to Prevent Postoperative Jejunal Ulcers by Aluminum Hydroxide Therapy: An Experimental Study in Mann-Williamson Dogs, *Am. J. Digest. Dis.* **5**:792, 1936.



In discussing the problem of fundusectomy in the treatment of peptic ulcer, Seeley and Tollinger,<sup>11</sup> after a series of observations on fundusectomized animals, concluded that fundusectomy had nothing to offer as a means of permanently reducing gastric acidity.

#### METHODS OF EXPERIMENTAL PROCEDURE

This investigation was divided into two experimental procedures. All animals were permitted to survive for their life span after (1) partial or "subtotal" gastrectomy with removal of three fourths of the stomach and diversion of the duodenal secretions, bile and pancreatic juice into the terminal portion of the

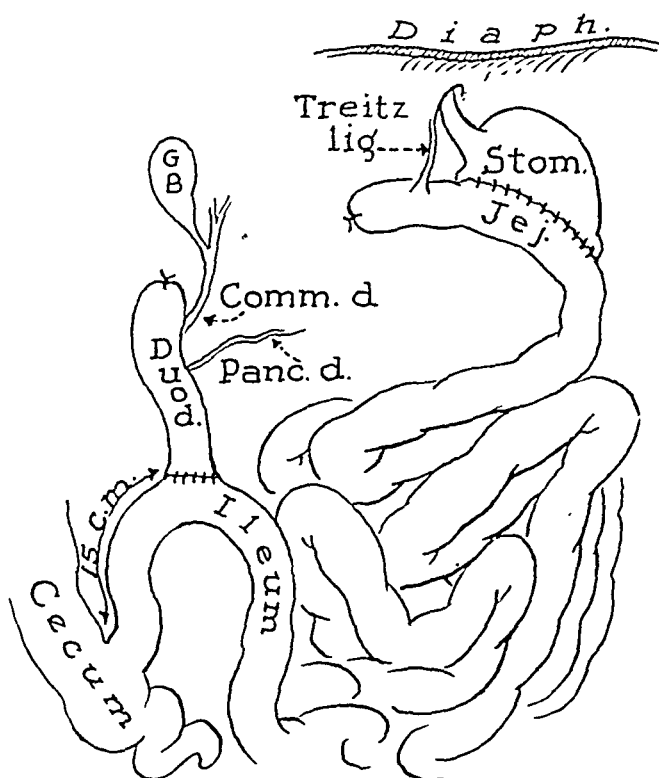


Fig. 1.—A partial or "subtotal" gastrectomy (leaving 25 per cent of the stomach), with anastomosis of the stomach to the jejunum was performed just distal to the ligament of Treitz. A Mann-Williamson operation was then performed, the distal portion of the duodenum being transplanted into the distal end of the ileum. (For results regarding ulcer formation, see table 1, series A.)

ileum and (2) "total" gastrectomy followed by shunting of the duodenal contents into the terminal end of the ileum. On arrival, all animals were quarantined for a period of ten days and placed on a stock diet of purina dog chow® and water. Preoperatively, no therapeutic or dietary measures were utilized to condition the animal. Postoperatively, diet consisted of milk for three days, after which they were fed a ration of pard,® 400 Gm.; ground raw pancreas, 200 Gm.; ground raw

11. Seeley, H., and Tollinger, R.: Fundusectomy in the Treatment of Peptic Ulcer, Surg., Gynec. & Obst. 61:155, 1935.

liver, 200 Gm., and milk, 200 cc. We used this improved diet because the experimental animals experienced great difficulty in maintaining their nutritional state on a diet of purina dog chow® alone and perished within too short a period (usually two weeks) for the results to be of statistical significance. It is evident that an experimental animal deprived of a stomach, and with its duodenal contents drained into the terminal portion of the ileum, is in dire need of all possible nutritional factors to prevent early death. However, no other postoperative medication or therapeutic measures were used. Animals surviving less than thirty days were not used in evaluating the results of our experiments, since it is clearly manifest that these animals had succumbed too soon after the operation to be used in the experiments; many of them died at operation.

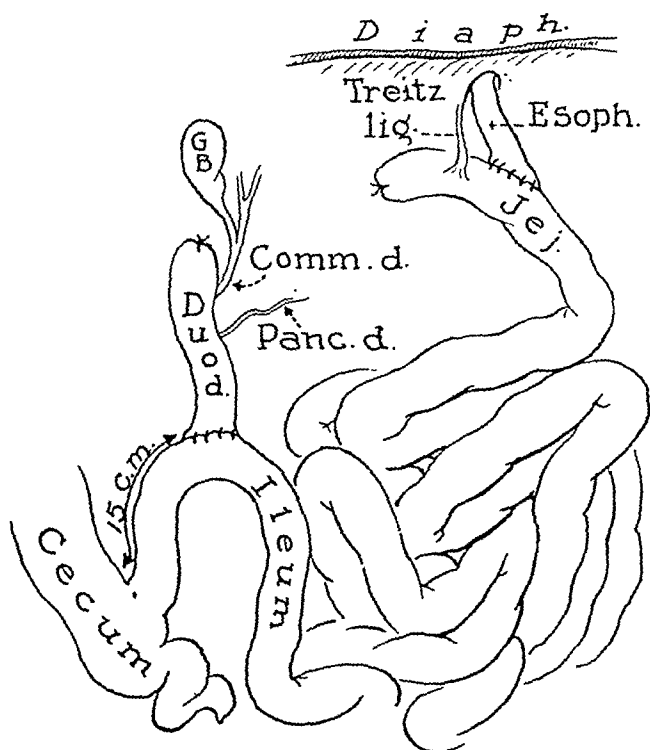


Fig. 2.—A "total gastrectomy" (except for a cuff 1 to 2 cm. wide) was performed, the esophagus or cuff of cardia being anastomosed to the jejunum just distal to the ligament of Treitz. At a second stage three weeks later, a Mann-Williamson operation anastomosing the terminal end of the duodenum to the ileum was performed. (For results regarding ulcer formation, see table 2, series B.)

*Series A. "Subtotal" Gastrectomy with Diversion of the Duodenal Secretions into the Terminal Portion of the Ileum.*—The first series comprises 10 animals subjected to a partial or "subtotal" gastrectomy and diversion of the duodenal secretions performed as follows: Under anesthesia produced by morphine and the intraperitoneal administration of pentobarbital sodium, the duodenum was transected at its pyloric juncture and the distal stump inverted. The jejunum was transected just distal to the duodenojejunal flexure at the ligament of Treitz. The distal limb of the jejunum was inverted and closed and the proximal limb sutured end to side into the terminal portion of the ileum, approximately 15 cm. from the

ileocecal juncture. Excision of the pylorus and 75 per cent of the fundus was then performed, with an end to side gastrojejunostomy (fig. 1). In this series, 4 animals survived the operation thirty days or more; the experimental data herein analyzed are derived only from this surviving group, which admittedly is small.

*Series B. "Total" Gastrectomy with Diversion of the Duodenal Secretions into the Terminal Portion of the Ileum.*—In this second experimental group, or series B, the operation was performed in two stages. In the first stage a "total" gastrectomy was performed as follows: Under morphine and intraperitoneal anesthesia, the duodenum was transected at its pyloric juncture and the distal stump inverted. The ligament of Treitz was incised, the duodenojejunal flexure being mobilized. The stomach was then totally extirpated (except for a small cuff of cardia), after which the cardia was anastomosed end to side into the jejunum, slightly distal to a point where the ligament of Treitz had crossed it. Because of the anatomic configuration of the diaphragm in the dog and the lack of mobility of the lower part of the esophagus, it is almost impossible for the animal to recover after absolute and total gastrectomy. However, only a small cuff of cardia just sufficient to allow for suturing to the jejunum remained. The width of the cuff

TABLE 1.—*Subtotal Gastrectomy with Duodenal Secretions Shunted into the Distal End of the Ileum*

Dog	Weight, Lb.	Date of Operation	Date of Death	Survival Time, Days	Weight Loss, Lb.	Comment
1	11	12/22/1946	1/24/1947	33	4	Jejunal ulcer 3 cm. by 8 mm.; ulcer not perforated; death due to inanition
2	20	12/27/1946	2/12/1947	47	8	Jejunal ulcer 1 cm. by 8 mm. not perforated
3	18	1/10/1947	3/13/1947	62	5	Jejunal ulcer 1.5 by 1.2 cm. perforated; peritonitis
4	21	1/24/1947	4/ 3/1947	68	6	Jejunal ulcer 1.4 by 1.2 cm. perforated; peritonitis

remaining approximated the width of the stomach clamp, usually 1 cm. This amount of cardia would represent less than 2 per cent of the total stomach. Our experience concurs with that of Mann<sup>12</sup> in this respect.

After a recovery period of approximately two to three weeks, the second stage, consisting of shunting of the duodenal secretions into the distal end of the ileum as previously described, was performed.

Eight animals survived both the preliminary complete gastrectomy and the subsequent operation for diversion of duodenal secretions into the terminal portion of the ileum. Only the data on experimental animals surviving the second operation thirty days or more are analyzed.

## RESULTS

*Series A.*—Among the 4 animals analyzed in this series, death occurred thirty-three, forty-seven, sixty-two and sixty-eight days respectively after operation, the average period of survival being fifty-two days (table 1). At necropsy all animals presented a stomal ulcer. In 2

12. Mann, F. C.: Gastrectomy: An Experimental Study, *Ann. Surg.* 95:455, 1932.

cases the ulcer had perforated, causing death by peritonitis. The ulcers were round or oval and sharply punched out with terraced edges, each step in the terrace representing successive invasion of the deeper layers of the jejunal wall, and the bases were hard and indurated. The ulcers were approximately 1 cm. in diameter, except for one which was oval in

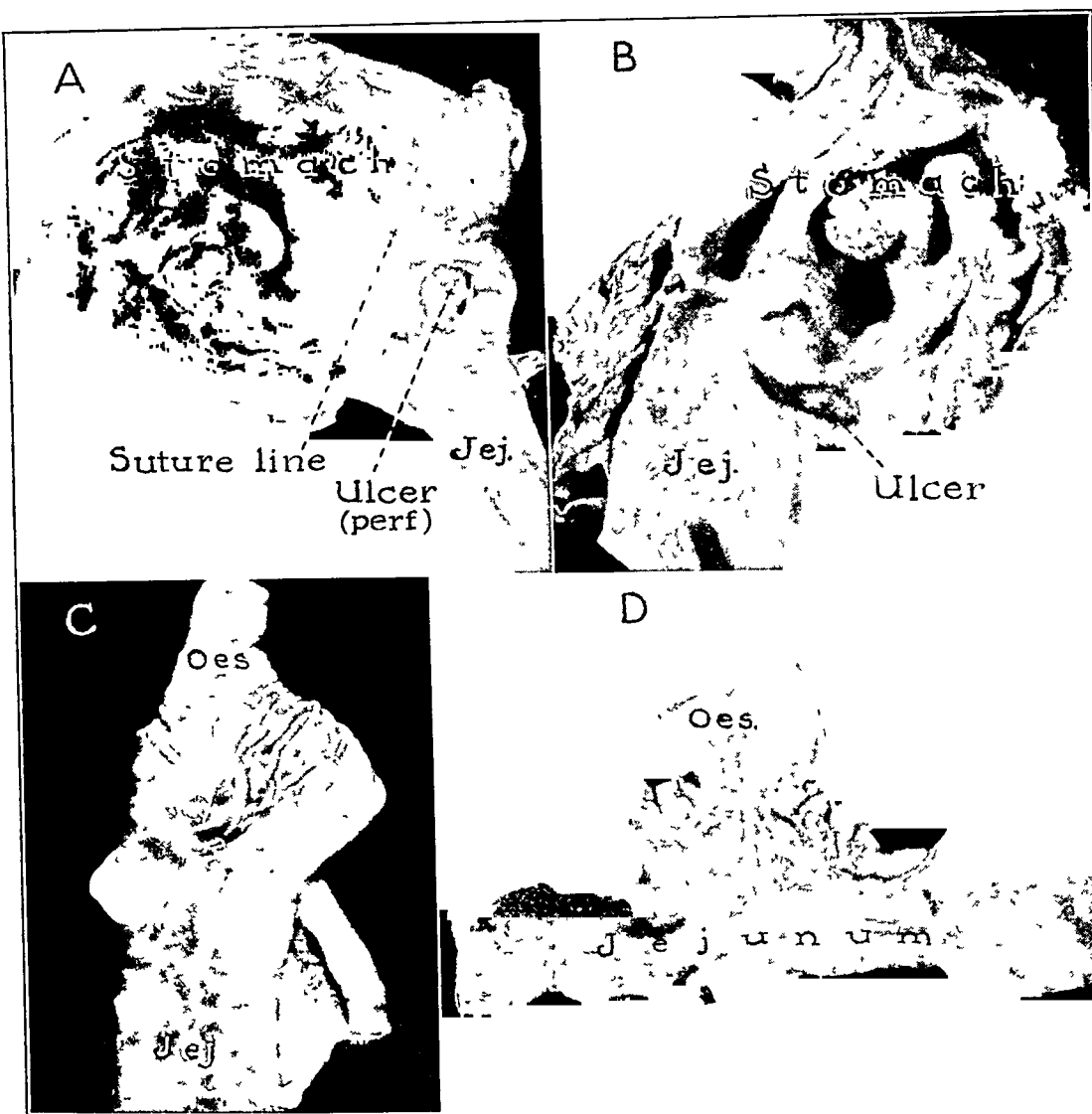


Fig. 3.—*A* and *B* represent autopsy specimen (dogs 3 and 1 respectively) revealing jejunal ulcers just distal to the suture line. In these animals three fourths of the stomach was removed, the stomach anastomosed to the jejunum as in figure 1 and a Mann-Williamson operation performed. *C* and *D* represent specimens removed from 2 animals (dogs 7 and 11 respectively) which underwent a "total" gastrectomy (except for a cuff 1 to 2 cm. wide) followed by a Mann-Williamson operation as shown in figure 2. No ulcer developed in any of the 8 animals. One of the animals (*C*) died one hundred and twenty days after operation because of inanition, another (*D*) was killed two hundred and twenty-three days after operation

outline and measured 3 cm. by 8 mm. All the ulcers were situated in the jejunal mucosa a few millimeters distal to the anastomotic suture line. At death all animals showed an average of 35 per cent loss of preoperative body weight. The remnants of all stomachs appeared hypertrophied and dilated and, while not assuming their former size, showed a perceptible increase in volume.

*Series B.*—As stated previously, in this series a "total" gastrectomy was performed first, and after an interval of a few weeks to allow for recovery the operation for shunting the duodenal secretions into the terminal portion of the ileum was performed. At the second operation, in addition to the usual adhesions, in some instances the duodenum was

TABLE 2.—*Total Gastrectomy Followed by Diversion of Duodenal Secretions into the Terminal End of the Ileum*

Dog	Weight, Lb.	Dates of Operations		Date of Death	Sur- vival Time, Days	Weight Loss, Lb.	Comment
		Gastrectomy	Internal Duodenal Drainage				
5	25	4/23/1947	5/ 9/1947	9/22/1947	134	12	No jejunal ulcer; jejunitis
6	25	4/25/1947	5/ 9/1947	11/21/1947	195	10	No jejunal ulcer; severe jejunitis; mucosa intact
7	19	5/ 2/1947	6/13/1947	10/10/1947	120	9	No jejunal ulcer
8	25	6/ 6/1947	8/ 3/1947	10/29/1947	87	10	No jejunal ulcer
9	20	8/29/1947	9/ 3/1947	10/20/1947	51	9	No jejunal ulcer
10	20	9/ 3/1947	9/17/1947	10/30/1947	44	7	No jejunal ulcer
11	21	3/19/1947	4/17/1947	11/25/1947 (killed)	223+	9	No jejunal ulcer; moderate degree of jejunitis; severe anemia
12	23	3/22/1947	4/16/1947	11/25/1947 (killed)	223+	10	No jejunal ulcer; severe anemia

found to be thickened and diffusely red, with mucosal hypertrophy. No hypertrophy or dilatation of the small amount of cardia was noted at this time. The jejunum did not show evidence of hypertrophy, dilatation or inflammation. It is possible that it was too early after the gastrectomy to note any changes in the gastrointestinal tract. The animals at this period had lost an average of 2 pounds (0.9 Kg.) in weight, or approximately 10 per cent of their preoperative body weight. The changes in the character of their stools were not unusually significant at this stage.

At death, after the two operations, all animals which survived thirty days or more showed marked evidence of nutritional imbalance, and some were extremely emaciated, with weight losses ranging from 40 to 50 per cent or more of their preoperative body weight (table 2). All animals consumed twice the amount of food necessary to maintain the body weight of a normal dog, yet the weight curve was downhill to an

extreme degree. The stools were large and voluminous, clay colored, soapy or putty-like in consistency and contained much undigested fat. No evidence of diarrhea or watery stool with admixture of blood was noted at any time.

At necropsy the complete absence of a gastric or jejunal stomal ulcer was noted in all experimental animals in this series. Further examination failed to reveal the presence of a possible healed ulcer. There was noted a slight dilatation of the jejunum opposite the remnant of gastric cardia, although the remnant did not appear dilated.

Microscopic sections of the cuff of cardia revealed the presence of oxyntic or acid parietal cells clearly up to the anatomic line of demarcation which marks the esophagogastric juncture. In this series of 8 experimental animals which survived the last operation for thirty days or more, death occurred in 6 animals forty-four, fifty-one, eighty-seven, one hundred and twenty, one hundred and thirty-four and one hundred and ninety-five days respectively after the second operation. At necropsy no stomal or jejunal ulcer was noted in the 6 animals; neither was there any evidence of a healed ulcer.

Two animals, nos. 10 and 11, were killed two hundred and twenty-three days after the second operation; no stomal ulcers were noted. The intestines in both animals were pigmented and of a deep buff color; all tissues and organs appeared extremely anemic.

I feel that the inclusion of additional food, particularly of the raw ground liver, in the diet played a significant role in keeping the animals alive. An incidental observation made during the course of this investigation revealed that if the raw ground liver was omitted from the diet, the downhill course of the animals was accelerated. Omission of the pancreas did not produce this effect.

#### COMMENT

Our studies on the effect of "subtotal" and "total" gastrectomy on the development of a stomal ulcer when the duodenal, biliary and pancreatic secretions are diverted into the terminal portion of the ileum indicate that the presence of more than 2 or 3 per cent of secreting stomach is necessary in the pathogenesis of the stomal ulcer. As stated previously, the animals in which only three fourths of the stomach was removed (series A) lived for an average of only fifty-two days after operation and succumbed to the effects of a stomal ulcer and inanition. On the contrary, the animals in series B, although subjected to a total gastrectomy, with diversion of the duodenal secretions, survived an average of one hundred and twenty-five days. (This includes 2 animals killed two hundred and twenty-three days after operation.) No special atten-

tion was given these animals except for a modification of their diet as described previously.

The animals in both series were subjected to a diversion of duodenal, biliary and pancreatic secretions into the terminal portion of the ileum, but stomal ulcers developed only in those animals which had approximately 25 per cent of their stomach intact (series A), with the consequent presence of acid and pepsin in the alimentary tract. Can the failure of a stomal ulcer to develop in the animals in series B ("total" gastrectomy) be explained on the basis of an absence of the duodenal contents in the face of the fact that the animals in series A underwent the identical operation for shunting duodenal contents but had only three fourths of the stomach removed? Ulcers developed in all instances in the latter series. One is led to the obvious conclusion that the presence of acid and pepsin is necessary and complementary in the development of a stomal ulcer. One must, of course, consider the antiulcer factors in the bile, duodenal secretions and pancreatic secretions. Although alkalinity has previously been considered the most important of these factors, evidence is accumulating that there may be other factors in these secretions. At any rate, the antiulcer factor in the bile cannot be strong since obstruction of the common duct is not accompanied with a duodenal ulcer. However, when duodenal and pancreatic secretions are excluded from the intestinal tract (as in a pancreatoduodenectomy for carcinoma of the head of the pancreas) a jejunal ulcer will form in a high percentage of cases. It is obvious that an excess amount of acid is not the sole cause of the ulcer, since the animals in series A had three fourths of the stomach removed and stomal ulcers developed. It is also noted that in spite of the fact that vagotomy abolishes the cephalic phase of gastric secretion and the amount of acid secreted, in experiments previously reported<sup>1</sup> stomal ulcers developed in all animals subjected to a vagotomy and the Mann-Williamson operation. Can this failure of the jejunum to protect itself against the development of a stomal ulcer in spite of the presence of a minimal amount of acid and pepsin, as noted in our experiments, be explained only on the basis of increased jejunal susceptibility? True enough there is clinical evidence of the increased susceptibility of the distal portion of the small intestine to ulceration by acid (even in minimal amounts) in the perforation of ulcers in a Meckel diverticulum containing gastric mucosa. However, in the experiments herein reported the animals in both series were subjected to the same type of shunting operation diverting duodenal secretions into the ileum; the only difference in the two series of experiments was that in one series practically all the stomach was removed whereas in the other series one fourth of the stomach remained. It is, therefore, obvious that the presence of gastric secretions was the important factor in the cause of the ulcer.

## SUMMARY

In the 4 animals in series A in which three fourths of the stomach was extirpated and the continuity of the alimentary tract restored by an end to side gastrojejunostomy followed by diversion of the duodenal secretions (including bile and pancreatic juice) into the terminal portion of the ileum, stomal ulcers developed and they all died. The average duration of life in this series was fifty-two days. In 2 of the 4 animals the ulcer perforated.

These are contrasted with the 8 experimental animals in series B, in which a "total" gastrectomy was performed, with anastomosis of the gastric cardia to the jejunum followed by shunting of the duodenal secretions into the terminal portion of the ileum. In none of the animals in this series did a jejunal or stomal ulcer develop, and neither was there any suggestion of a healed stomal ulcer. Of the 8 animals in this series, 6 succumbed forty-four, fifty-one, eighty-seven, one hundred and twenty, one hundred and thirty-four and one hundred and ninety-five days after the second operation. Two animals (nos. 11 and 12) were killed two hundred and twenty-three days after operation. The average survival period for the animals in this group was one hundred and twenty-five days (including the 2 which were killed). All animals presented varying degrees of jejunitis, and the tissues appeared extremely anemic. The weight loss for the animals in this group averaged 45 per cent of their preoperative body weight. It is probable that with care the animals in series B could have lived indefinitely, but no particular attention was paid to their nutrition except for a modification of their stock diet.

## CONCLUSION

From these data it is concluded that the presence of gastric secretion is the important factor in the development of an ulcer after a Mann-Williamson operation has been performed, so far as no ulcer will develop if all (at least 98 per cent) of the stomach is removed.

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# EFFECTS OF VAGOTOMY IN THE RAT

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**S**TUDIES concerning the effects of section of the vagi are numerous and date back to the sixteenth century. In 1883, on the basis of his own experiments and from an extensive review of previous literature, Heidenhain<sup>1</sup> emphasized that bilateral vagotomy performed in the neck was inevitably fatal, yet when done below the diaphragm it appeared to be a rather harmless operation. It remained, however, according to Pavlov,<sup>2</sup> for Krehl<sup>3</sup> in Ludwig's laboratory to evaluate properly the effect of double vagotomy on survival time. He clearly established that animals can survive bilateral section of the vagus below the lung root but invariably succumb after such section in the neck. Later experiments on dogs, cats and rabbits<sup>4</sup> and the more recent ones of Ferguson<sup>5</sup> on monkeys amply confirmed the results of these investigators. No generally acceptable explanation is, however, as yet available for the fact that this operation, when performed in the neck, is inevitably

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From Fels Research Institute, Temple University School of Medicine.

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fatal unless extraordinary measures are applied.<sup>6</sup> Pavlov's school holds that of the numerous effects of vagotomy believed to be the cause of death following bilateral section in the neck the most important and hardest to control is the pronounced impairment of the functions of the digestive system. This results from the elimination of the nervous control of gastric, pancreatic and possibly also intestinal secretions plus impairment of motility of the esophagus and stomach, which lead to inadequate digestion and nutrition. When the effects (stagnation, putrefaction of food in the stomach and esophagus and aspiration pneumonia) of these altered functions were allayed through specific measures, Pavlov found that dogs vagotomized at any level could be made to survive indefinitely. These measures could be applied only if the animals were esophagotomized and provided with a gastric fistula.

Pavlov and his associates, as well as some of their predecessors, attributed better survival of animals vagotomized below the lung root to the anatomic difficulties in achieving complete vagotomy at this level. Aside from the difficulty of severing all free vagal fibers below the lung root, the entrance of some vagal branches above this level into the esophageal wall and their passage through it to the stomach were thought to be highly probable. These factors would make complete severance of all vagal fibers at this level well nigh impossible. Only complete and consistent absence of acid gastric secretion in response to sham feeding in repeated trials could, according to Pavlov, be accepted as conclusive evidence of complete severance of vagal innervation to the stomach.

It is not our purpose in this paper to review clinical experiences in bilateral vagotomy, but there appears to be a sharp difference of opinion regarding the possibility—in man, too—of achieving complete severance of all vagus fibers below the lung root. Some<sup>7</sup> are in agreement with the view regarding the anatomic difficulties expressed by Pavlov. Others<sup>8</sup> believe that complete severance of all vagal fibers at this level can be effectively accomplished.

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The rather recent extensive application of bilateral resection of the vagus to the treatment of gastric and duodenal ulcer makes a more complete experimental study of the manifold effects of this operation imperative.

To the best of our knowledge, no observations have been reported concerning the effects of vagotomy on rats. Our primary interest in this problem was to establish the role of the vagi in interdigestive gastric secretion. In addition, we were also concerned with the possible effects of vagotomy on the motor functions of the gastrointestinal tract and on the nutrition and well-being of the animals. The rat is especially valuable for such investigations since it is widely used in nutrition studies and its stomach has recently been shown to be so readily the site of true peptic ulceration.<sup>9</sup>

#### EXPERIMENTS

*The Technic of Vagotomy.*—Wistar strain rats, chiefly male, weighing 150 to 180 Gm., which had been grown in our own colony were subjected to transdiaphragmatic resection of the vagus nerve. The following technic was used:

The animal is anesthetized with ether and placed on its right side. An incision 1 to 1½ inches (2.54 to 3.81 cm.) long, beginning at the linea parasternalis, is made on the left side of the abdomen 3 to 5 mm. below the ribs. Urethane (0.9 cc. of 10 per cent solution per hundred grams of weight) is injected into the cecum, and the stomach and spleen are withdrawn. After the left lobe of the liver is displaced to the right, the esophagus is clearly exposed and the vagus trunks, both right and left (actually lying somewhat anteriorly and posteriorly respectively), can be seen as well as a plexus formation about midway between the diaphragm and the cardia. Each trunk just above the plexus is lifted from the esophagus with a fine forceps and isolated with a fine hook, damage to the blood vessels being avoided. In order to achieve vagus resection, each vagus nerve trunk is pulled downward into the abdomen

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as far as possible, and the longest possible segment (never less than 1 cm.) is excised from the level of the diaphragm to the cardia. After proper resection, the upper stump should, at biopsy or autopsy, be found in the thoracic cavity, 7 to 10 mm. above the diaphragm. In about 90 per cent of the rats, two single vagal trunks emerge beneath the diaphragm. Occasionally, one or two additional small branches also emerge. They can be detected later at autopsy only by careful examination through a magnifying glass. These branches, therefore, may escape resection. In cases of incomplete vagotomy the effects on gastric secretion, motility and survival are strikingly different from those following complete vagotomy.

After the resection of the nerves is completed, the organs are replaced in the abdominal cavity and the wound is closed in the usual manner.

Operations performed in addition to vagotomy, depending on the type of experiment, included pyloric ligation, production of a gastric fistula, exteriorization of a portion of the cecal wall and esophagotomy.

*The Effects of Vagotomy on Spontaneous Gastric Secretion.*—Rats were fasted for a period long enough for previously ingested food to be completely digested and absorbed (eighteen to seventy-two hours), with water allowed ad libitum. They exhibited a considerable spontaneous secretion of gastric juice which had a composition similar to that induced by sham feeding. Acidity, pepsin content and rate of this secretion depended to a large extent on the conditions of the experiment; in unanesthetized animals this "interdigestive secretion" was greater in amount and was rather labile when compared with that of the anesthetized animals. The rate of secretion was influenced by the depth of anesthesia. These observations alone indicate the importance of the nervous mechanism in this phase of gastric secretion. That parasympathetic innervation is especially concerned is evidenced by the effect of atropinization on the secretion.<sup>10</sup>

Friedman<sup>11</sup> reported that spontaneous secretion in the rat is not affected by atropine, but we have found that sufficiently large doses of atropine did inhibit it almost completely. However, the effects of atropine are manifold, and the dosage required to cause marked inhibition was so large that more direct experiments were necessary to establish the exact role of the vagi in controlling spontaneous secretion in rats.

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10. Komarov, S. A.; Shay, H.; Rayport, M., and Fels, S. S.: Some Observations on Gastric Secretion in Normal Rats, *Gastroenterology*, **3**:406, 1944.

11. Friedman, M. H. F.: Histamine Ineffective in the Rat as a Gastric Secretory Stimulant, *Proc. Soc. Exper. Biol. & Med.* **54**:42, 1943.

We have studied the immediate and remote effects of both complete and partial vagotomy.

*The Immediate Effects of Vagotomy on Gastric Secretion.*—Two technics were employed in studying the immediate effects. One had the advantages of simplicity and minimum surgical trauma since, in addition to vagotomy, it involved only pyloric ligation and exposure of the cecum. This procedure did not, however, prevent contamination of the gastric juice by saliva or other extraneous matter (feces or hair). Such contamination was avoided in the second method, which included esophagotomy in addition to the aforementioned procedures.

*Experiments with Simple Pyloric Ligation.*—The technic employed is similar to that previously described for the experimental production of gastric ulceration in rats.<sup>9</sup>

Animals weighing 150 to 180 Gm. are fasted for forty-eight hours but allowed water ad libitum. They are anesthetized with ether. Through a midline incision 5 to 8 mm. long below the umbilicus, a small portion of the cecal wall is exteriorized and urethane injected. Then through a left subcostal incision 3 to 4 cm. in length one or both vagi are resected as described previously, and the pylorus is ligated. The wound is sutured, and the animals are left in clean cages overnight for seventeen to nineteen hours. They are then anesthetized by the intracecal injection of pentobarbital sodium and killed. The abdomen is opened and a ligature placed around the esophagus. The stomach is removed, and its contents are drained into a graduated centrifuge tube through a nick in the wall of the stomach along the greater curvature proximal to the pyloric ligature. The contents of each stomach were individually analyzed as described in the following paragraphs.

*Analysis of Gastric Contents.*—The specimens were centrifuged in a graduated centrifuge tube at 2,000 revolutions per minute for ten minutes and the respective volumes of supernatant and solid materials recorded. The rate of secretion is expressed in cubic centimeters per hour per hundred grams of body weight, which was calculated from the volume of supernatant fluid. The supernatant fluid was pipetted off and the hydrogen ion concentration, free and total acid, total chlorides and pepsin were determined by routine methods used in this laboratory.<sup>12</sup>

Groups of 4 to 6 animals were used for each experiment. Controls were included in each group. Control animals were treated exactly like the vagotomized animals except that their vagi were "handled" but not sectioned.

The results showing only mean values are presented in table 1. The results are so unequivocal that no elaborate statistical analysis appears necessary.

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12. Komarov and others.<sup>10</sup> Shay and others.<sup>9</sup>

Bilateral vagotomy produced an average reduction in the rate of secretion to 41 per cent of that in the controls, while unilateral vagotomy reduced it to 78 per cent. It is noteworthy that in no animal subjected to bilateral vagotomy was free acid present in the stomach. The relatively low figures for total chloride in the gastric contents of animals which underwent unilateral and, particularly, bilateral vagotomy indicated a considerable contamination of the gastric contents with saliva and that such contamination was proportionately greater in animals subjected to bilateral vagotomy than in those subjected to resection of one vagus nerve. This is probably due to the greater reduction in gastric secretion in the former, since it is not likely that these animals swallowed more saliva than the latter.

TABLE 1.—*Immediate Effect of Vagotomy on Gastric Secretion (Animals Not Subjected to Esophagotomy)*

	Control ↓	Vagotomy		
		Single		
		Left	Right	Double
Number of animals.....	20	15	16	15
Rate, ml./hr./100 Gm.....	0.265	0.217	0.198	0.109
pH .....	1.76	1.83	1.80	3.89
Acidity, mEq./liter				
Total.....	77	73	79	31
Free.....	31	25	27	0
Chloride, mEq./liter.....	148	133	145	110
Pepsin, Mett units.....	189	145	180	107

Results produced by the section of one vagus nerve were essentially the same whether the left or right nerve was severed.

*Experiments with Pyloric Ligature and Esophagotomy.*—The experimental technic used in this group was the same as that used in the preceding series except that after exteriorization of a small portion of the cecal wall and injection of urethane esophagotomy was performed. The esophagus was exposed by an incision 1 cm. long just above the sternum, slightly to the left of the midline, ligated with a fine thread as far aborally as possible and cut just above the ligature. The proximal end of the cut esophagus was sutured into the upper end of the incision and the rest of the wound closed. Only then were the vagi resected and the pylorus ligated.

Esophagotomy increases the operative time only about five minutes. While additional trauma in a highly sensitive region undoubtedly aggravated operative shock, it did not inhibit spontaneous secretion in the control animals. This can be seen by comparing the results in table 1 with those in table 2. The number of experiments in this group was

not so large as in the previous one, since individual variations in this series were even less notable than in the first.

Figures for total chloride (table 2) indicate that the gastric juice was only slightly contaminated, if at all, so that the results observed reflect the actual secretory activity of the stomach. Bilateral vagotomy abolished secretion so nearly completely that sufficient gastric contents were not available for complete analysis; only the rate of secretion and the  $p_H$  could be determined in each animal, while only a few scattered determinations were possible on acidity and chloride and none on pepsin.

Again results produced by resection of the vagus on the right or left side were practically identical. Unilateral vagotomy reduced the rate of secretion to about one third and the output of free acid to approximately one fourth of the control values without otherwise materially altering the composition of the secretion. These changes were accompanied with

TABLE 2.—*Immediate Effect of Vagotomy on Gastric Secretion (Animals Subjected to Esophagotomy)*

	Control ↓	Vagotomy		
		Single		Double
		Left	Right	
Number of animals.....	9	6	7	7
Rate, cc./hr./100 Gm.....	0.244	0.082	0.085	<0.01
$p_H$ .....	1.24	1.42	1.41	2.74
Acidity, mEq./liter				
Total.....	89	92	96	85
Free.....	77	55	51	30
Chloride, mEq./liter.....	150	148	154	153
Pepsin, Mett units.....	205	238	208	Quantity not sufficient

a correspondingly higher  $p_H$  in the secretion of the vagotomized animals. Some increase in the pepsin content of the animals subjected to section of the left vagus nerve does not appear significant.

These results indicate that unilateral vagotomy depressed the rate of secretion considerably while bilateral vagotomy inhibited gastric secretion completely, or nearly so. The small amounts of gastric juice (0.1 to 0.2 cc.) recovered from the group subjected to the latter at the end of the eighteen hour period could represent secretion remaining in the stomach at the time of pyloric ligation.

The most striking difference between the results in animals which were subjected to esophagotomy and in those which were not was the failure of bilateral vagotomy to abolish gastric secretion in the latter series. This may be due to the gastric secretagogue action of saliva in these animals, since Sokolov<sup>18</sup> showed such an action for saliva when

13. Sokolov, A. P.: *Analysis of the Secretory Action of the Stomach in the Dog*, Thesis, St. Petersburg, F. Vaisberg and P. Gershunin, 1904.

it is introduced into the whole, isolated stomach, and Savich and Zeljony<sup>14</sup> demonstrated that sodium carbonate, a constituent of saliva, excites gastric secretion when placed in contact with pyloric mucosa. Our results indicate that, in the rat, saliva may act as a secretagogue in the absence of vagal innervation.

#### THE EFFECTS OF ACUTE VAGOTOMY ON FORMATION OF ULCER

Normal animals subjected to pyloric ligation when the stomach is empty always develop extensive gastric ulceration,<sup>9</sup> which is mostly confined to the rumen and, to a lesser degree, also involves the body and antrum of the stomach. In all control animals severe ulcerations developed; some had so many it was impossible to count them. Nine animals comprising the control group (table 2) had several hundred ulcerations, many of them perforated. Of 13 animals subjected to unilateral vagotomy, 6 had no ulcers and the remaining 7 had eight tiny ulcerations in all, of which six were located in the rumen. No ulcerations were found in the animals subjected to bilateral vagotomy, while ulceration was much less pronounced in those in which one vagus nerve was resected than in the control animals. The results in the animals which underwent complete vagotomy are readily explained by the almost complete absence of secretion in the stomach. Although the number of ulcers were not counted as thoroughly in the groups represented in table 1, similar results were observed.

#### REMOTE EFFECTS OF VAGOTOMY ON GASTRIC SECRETION

At first we experienced difficulties in keeping completely vagotomized rats alive longer than three or four days. The animals withstood the operation well, taking water and milk the first day postoperatively. On the second or third day they appeared vigorous and eagerly ate solid food. When placed on our diet of purina checkers,<sup>®</sup> they refused food on the third or fourth day postoperatively and soon died, none surviving more than a week. At autopsy the stomachs of all these animals were found distended with large masses of food. The esophagus was also full of food, as well as the mouth cavity and the nostrils, and occasionally food particles were found in the trachea. However, the small intestine was empty of chyme, and little feces was present in the cecum and colon. Evidently gastric secretory and motor functions were so impaired that adequate digestion was not possible. While searching for a solution to this nutritional problem, we lost more than 50 vagotomized animals. Suffice it to mention here that by using a diet consisting

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14. Savich, V., and Zeljony, G.: Zur Physiologie des Pylorus, Arch. f. d. ges. Physiol. **150**:128, 1913.



in part of predigested food, we maintained completely vagotomized animals in reasonably good condition for many weeks, the longest period of survival being one hundred and twenty days for 1 animal at the time it was killed.

In these experiments we also employed two technics. In one series the effects of vagotomy on gastric secretion were studied after pyloric ligation alone. In the other the animals were esophagotomized and both gastric and cecal fistulas were made in addition to ligation of the pylorus.

In the first series 3 groups of animals were studied: control animals, those subjected to incomplete vagotomy and those subjected to complete vagotomy. Incomplete vagotomy occurred by accident rather than by design. In some animals the vagal trunks were so well developed that we decided not to destroy the esophageal plexus and only excised the usual length of the trunks. Subsequent autopsies on these animals disclosed well developed neuromas (3 to 7 mm.) at the proximal end of the divided nerve as well as definite strands of nerve tissue extending from the neuromas toward the stomach. In other animals a small branch of the vagus, usually on the right side of the esophagus, escaped detection during the operation and was not excised. In the "complete vagotomy" group, all visible fibers of the esophageal plexus were excised in addition to resection of both vagal trunks, and no uncut fibers or signs of regeneration were found at autopsy. All vagotomized animals accumulated hair in the stomach. This was removed through a small incision in the rumen at the beginning of the period of starvation, forty-eight hours before the actual experiment. On the day of the experiment the pylorus was ligated through the usual midline incision, with the animals under ether anesthesia. The animals recovered from the anesthesia almost immediately after the wound was closed. They were killed six hours after pyloric ligation, and the gastric contents were collected as described previously.

The results obtained with this technic are given in table 3; they closely resemble those obtained in the experiments testing the immediate effects of acute vagotomy on animals not subjected to esophagotomy. Complete vagotomy performed twelve to twenty-nine days before the experiment resulted in a decrease in the rate of secretion to about one third, in the output of total acid to approximately one eleventh and in pepsin output to about one fourth of that of the control animals. There was a decrease in the amount of free acid to zero. Incomplete vagotomy performed eighteen to thirty-eight days before testing also produced a striking decrease in gastric secretion: diminution of the rate to about one half and a considerable lowering of acidity, especially

of free acid. The change, however, was not as striking as that following complete vagotomy. Low figures for total chloride in the completely vagotomized group suggest considerable contamination of the gastric contents with saliva. This may, also in these experiments, be partly responsible for the relatively high secretion.

Esophagotomy and the production of gastric and cecal fistulas, in addition to pyloric ligation, were employed in a number of animals surviving complete vagotomy for periods of from twelve to one hundred

TABLE 3.—*Remote Effect of Vagotomy on Gastric Secretion (Animals Subjected to Pyloric Ligature Only)*

Days Post- opera- tively	Weight Gain, Gm./Day	Rate, Cc./Hr./ 100 Gm.	pH	Acidity		Chloride, MEq./ Liter	Pepsin, Mett Units	Hair, Cc./Day
				MEq./Liter				
				Total	Free			
Control								
19	+0.42	0.81	1.18	105	72	157	100	None
19	+0.21	0.52	1.17	100	74	152	77	None
19	+1.10	1.04	1.12	113	82	156	154	None
29	+0.55	0.71	1.22	106	69	147	36	None
29	+1.00	0.93	1.18	121	73	155	52	None
Mean.....		0.80	1.17	109	74	153	84	None
Mean output *.....		....	....	87	59	...	67	None
Incomplete Vagotomy								
29	-0.60	0.30	2.81	68	0	150	135	0.035
36	-0.22	0.58	1.49	78	35	152	196	0.083
38	0	0.34	3.53	68	0	163	207	0.079
18	-1.80	0.34	1.74	90	24	161	353	0.050
Mean.....		0.39	2.03	76	15	...	223	....
Mean output.....		....	....	30	6	...	87	....
Complete Vagotomy								
12	-3.30	0.27	4.65	28	0	100	31	0.080
12	-4.00	0.34	7.08	0	0	120	8	0.050
12	-4.80	0.27	3.87	46	0	133	85	0.040
12	-2.80	0.23	3.07	42	0	144	108	0.070
29	-2.00	0.19	3.51	44	0	...	125	0.024
Mean.....		0.26	3.66	32	0	126	71	....
Mean output.....		....	....	8	0	...	19	....

\* Mean output indicates acidity expressed as milliequivalents per hour per hundred grams and pepsin expressed as Mett units per hour per hundred grams.

and six days and in a corresponding number of control animals. It was necessary in vagotomized animals surviving for more than a month to remove balls of accumulated hair surgically through a small incision in the rumen. This procedure had to be repeated every three to four weeks. Control animals were treated similarly, although no hair was present in the stomach. In each of these animals a gastric fistula was made and the cecum partially exteriorized about one week before the experiment. The animals were starved twenty-four or forty-eight hours before esophagotomy was performed; with the animals under urethane anesthesia the pylorus was tied and gastric secretion was collected for

sixteen to twenty-four hours. Some of them were trained to stand handling without anesthesia and were subjected to sham feeding experiments. The results are summarized in table 4.

This table indicates that the rate of spontaneous gastric secretion in animals surviving complete vagotomy from twelve to one hundred and six days was reduced to about one fourth that in control animals and free acidity was approximately 10 per cent lower, with corresponding changes in  $p_{\text{H}}$ . Sham feeding produced no effect in the vagotomized rats, while the stomachs of control animals responded with characteristically increased secretion.

It will be noted that in these series the rate of secretion was considerably lower in both vagotomized and control animals (table 4) than in those animals in which pyloric ligation only had been used

TABLE 4.—*Remote Effect of Vagotomy on Gastric Secretion (Animals Subjected to Esophagotomy, Pyloric Ligature and Gastric and Cecal Fistula)*

	Number of Animals	Rate, Cc./Hr./ 100 Gm.	<i>p</i> <sub>H</sub>	Acidity		Chloride, MEq./ Liter	Pepsin, Mett Units
				MEq./Liter Total	Free		
A. Interdigestive Phase							
Control.....	10	0.156	1.40	84	46	152	130
Vagotomy.....	13	0.039	2.05	97	41	...	...
B. Sham Feeding Phase							
Control							
C*.....	2	0.090	2.11	40	25	...	...
SHF†.....		0.270	1.51	64	39	...	452
Vagotomy							
C*.....	5	0.032	2.23	..	..	...	...
SHF†.....		0.030	2.27	..	..	...	...

\* C indicates control period.

† SHF indicates sham feeding period.

(table 3). The higher rate of secretion in the latter group may be due either to less operative shock or to stimulation by saliva or both. The following conclusions concerning the effects of vagotomy on the spontaneous or "interdigestive phase" of gastric secretion in rats are, we believe, justified:

1. Acute complete vagotomy abolishes spontaneous secretion. Unilateral vagotomy inhibits it considerably, especially if entrance into the stomach of extraneous materials is prevented by esophagotomy.

2. Some restoration of spontaneous secretion occurs in animals surviving complete vagotomy for several weeks, but this secretion is exceedingly small and is probably produced by a humoral mechanism, since it is not affected by sham feeding. Incomplete vagotomy also produces a considerable reduction of spontaneous secretion.

## OTHER REMOTE EFFECTS OF COMPLETE BILATERAL VAGOTOMY

*Conditions for Survival.*—We stated previously that completely vagotomized rats do not survive more than a week when placed on a diet of purina checkers,<sup>®</sup> powdered or whole.

The addition of choline hydrochloride to the drinking water prolonged the survival time of vagotomized rats on a purina<sup>®</sup> diet to as long as three weeks if each animal consumed 100 to 150 mg. (50 to 100 mg. per hundred grams of body weight) of the drug daily. This dosage proved to be toxic. The animals frequently became cyanotic and apparently suffered intestinal cramps. They did not thrive and lost weight. At biopsy or autopsy the accumulation of solids in the stomach was not so pronounced as in animals kept on the same diet without choline (fig. 2).

Only if the diet contained predigested proteins as a source of nitrogen and starch or sucrose as carbohydrate was it possible to keep vagotomized animals alive indefinitely. Starch was found to be superior to sucrose since it permitted the animals to keep themselves clean more easily and so prevented a too rapid accumulation of hair in the stomach. The final experimental diet used was as follows:

Liver powder (Wilson).....	4%
Lactamin <sup>®</sup> (protein hydrolysate).....	30%
Crisco <sup>®</sup> .....	8%
Salts (Steenboch) <sup>15</sup> .....	4%
Vitamins A and D (natural vitamin oil).....	2%
Corn oil (Mazola).....	2%
B Plex <sup>®</sup> (Wyeth).....	2%
Corn starch.....	48%
Vitamin K.....	10 mg. per thousand grams of diet

OTHER ABNORMALITIES IN THE DIGESTIVE TRACT FOLLOWING  
BILATERAL VAGOTOMY

The esophagus below the lung root was always enlarged, even when empty. While in the control animals its diameter was about 2 mm., in completely vagotomized animals it was always more than 5 mm. when empty and even wider when filled with air, saliva or gastric juice. When the esophagus was filled with food masses, it was occasionally as large as 10 mm. in diameter. In some cases the esophagus was distended even in the neck. It was frequently filled with food in living animals. In addition, completely vagotomized animals readily tended to regurgitate gastric contents into the mouth cavity. This phenomenon was never observed in normal rats. Transit of food through the esophagus was apparently also disturbed, since the esophagus of many vagotomized rats at autopsy was filled with well masticated food masses which were alkaline in reaction. By contrast with the esophagus, the cardia appeared constricted. Actually this was not so, since in most

15. Steenboch, H., and Nelson, E. M.: Fat Soluble Vitamins: XIII. Light in its Relation to Ophthalmia and Growth, *J. Biol. Chem.* **56**:355, 1923.

cases the diameter of the cardia was 2.5 mm., while in the control animals it measured 2 mm. The function of the cardia, however, appeared to be impaired. Its appearance suggested a state of fixed incomplete closure. On biopsy, the stomach was always found to be much larger than normal and flabby in appearance even when it was empty. The pylorus nearly always appeared contracted. The small intestines of animals which had succumbed without being subjected to experimentation contained little or no chyme, even if the stomach contained food, and the frequent occurrence of neutral or alkaline reaction in the intestines—a phenomenon observed in few normal animals—was striking. At all biopsies or autopsies the cecum and colon contained little feces.

These findings indicate a severe impairment of the motor functions of the esophagus, cardia, stomach and pylorus. Changes in the

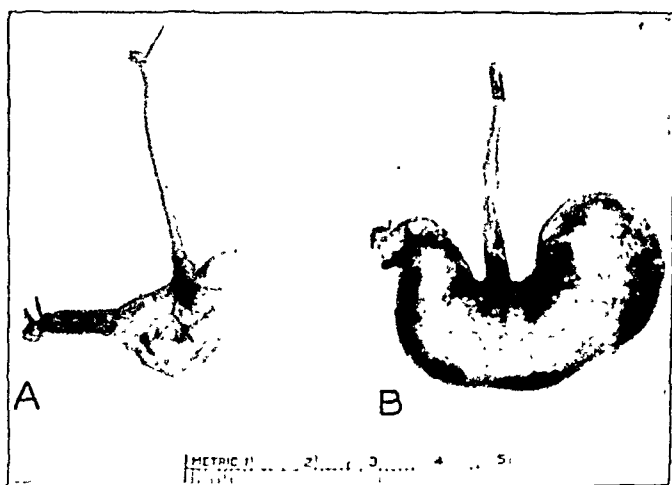


Fig. 1.—*A*, stomach and esophagus of control animal on colony diet of purina checkers—forty-eight hours of starvation except for water before being killed. *B*, stomach and esophagus of animal after bilateral transdiaphragmatic vagotomy. Animal maintained on colony diet of purina checkers for five days followed by forty-eight hours of starvation before being killed. Note the empty appearance of the stomach of the control animal in contrast to the distended stomach of the vagotomized animal. The reason for the distention is seen in the large food mass in the opened stomach in figure 2. Both animals were the same age and weight.

intestines may or may not be secondary—at present we have no basis on which to form any definite conclusions. The accompanying photographs illustrate some of the changes.

It should be added that the incidence of pathologic changes in the lungs was high in vagotomized animals. Many autopsies showed spotty congestion and hemorrhagic infiltration of both lungs, which in most cases was confined chiefly to the lower lobes. In some cases both lungs appeared to be diffusely infiltrated. Such abnormalities were not observed in the control animals.

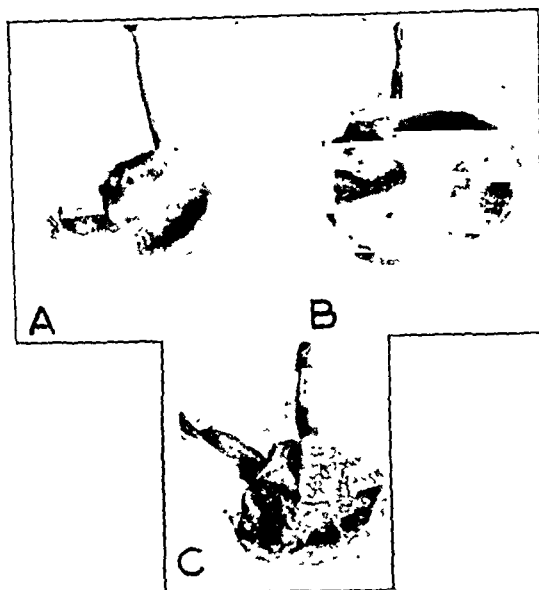


Fig. 2.—Stomach laid open after incision along greater curvature. Weights of animals,  $120 \text{ Gm.} \pm 10 \text{ Gm.}$  *A*, same as in figure 1. Stomach completely empty. *B*, same as in figure 1. The large mass of food explains the distended appearance in figure 1. *C*, same as in *B*, except that animal received choline, 50 mg. per hundred grams of body weight daily, from the day of vagotomy. The improved motor function of the stomach over that of *B* is apparent.

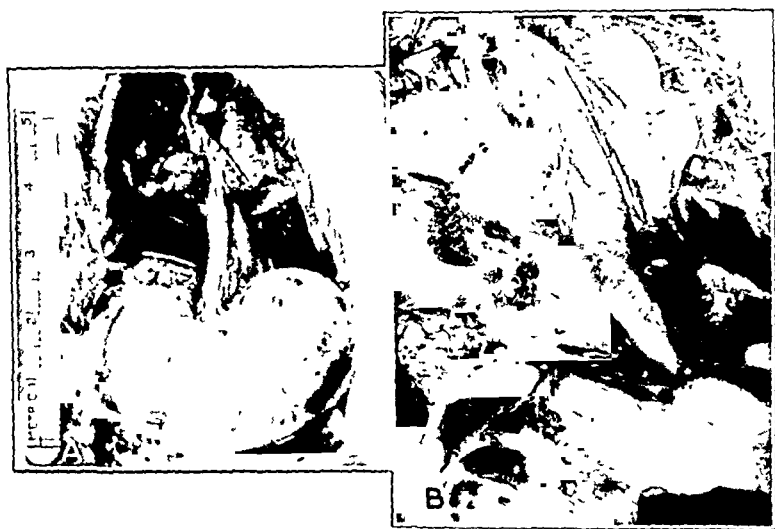


Fig. 3.—*A*, control animal, with vagi intact, after forty-eight hours of starvation. Esophageal fistula in neck; pylorus ligated. Animal was killed nineteen hours after pyloric ligation. Note the usual result after such procedure. The stomach is distended with gastric secretion, and typical ulcerated areas are visible in the rumen through the serosal surface. *B*, same procedures as in control animal in *A* except that this animal had bilateral transdiaphragmatic vagotomy done one hundred and five days previously. Note the collapsed state of the stomach, which obviously had secreted little gastric juice in the nineteen hour period following pyloric ligation. In spite of the small quantity of gastric secretion, note the dilatation of the entire esophagus and the relatively narrowed appearance of the cardia.

## NUTRITION

The partially predigested diet which we were forced to use in these experiments did not appear to be as adequate as we should have liked. Although the control animals gained weight steadily, their rate of increase was much less than that obtained in normal rats of the same age on our house diet. Furthermore, their fur did not remain as smooth as that of animals on a completely satisfactory diet. Vagotomized animals on the experimental diet as a rule lost weight or only barely maintained it, while few showed any gain in weight (table 3). These results indicate that the profound changes incident to complete vagotomy interfere with the proper utilization of even predigested food.

Studies conducted on the rat with Dr. R. Kolm and Dr. L. Edwards, to be detailed elsewhere, show the digestion and absorption of fats and the storage of glycogen by the liver to be unaffected by complete vagotomy.

## COMMENT

Our results show that the immediate effect of bilateral trans-diaphragmatic vagotomy in the rat is almost complete cessation of spontaneous gastric secretion. McCrea and his associates<sup>4</sup> have ascribed certain other immediate effects of bilateral vagotomy on gastric motility to the narcosis and shock incidental to vagotomy and not to the severance of vagal innervation. Such a mechanism cannot be held responsible for the inhibition of gastric secretion in our experiments since (1) control animals were treated exactly as the vagotomized animals in every detail except that vagotomy was not performed and (2) inhibition of secretion was permanent as long as the animals were allowed to survive. The results of our experiments on rats are in good agreement with those of Pavlov and his associates on dogs, in which the function of the vagi as the true secretory nerves for the gastric glands was first established. An analysis of our data, furthermore, places the mechanism of spontaneous gastric secretion in the unanesthetized fasting rat almost completely under nervous (vagus) control, with the possibility that humoral factors may contribute a small part in the mechanism of this secretion. The constant presence of bile in the intestine of the rat, as previously mentioned,<sup>10</sup> may be responsible, at least in part, for the humoral part of the mechanism.

Unilateral vagotomy in the rat produced results which forced us to conclusions that are in sharp contrast with the view expressed by many investigators that partial vagotomy fails to influence gastric secretion or only causes some initial inhibition followed by complete restoration of secretory function. In the rat, incomplete vagotomy is followed by a substantial and persistent decrease in the rate and acidity of spontaneous secretion. These changes promptly follow the operation and render a

high degree of protection against ulceration following pyloric ligation under conditions which produce uniform ulceration in animals with both vagi intact.

Finally we would emphasize the fact that a truly complete vagotomy below the lung root in the rat is a fatal operation unless extraordinary measures are taken to enable the animals to survive. They can survive for a long period if a special diet is used which overcomes the decided impairment of gastric motor function. Even when this is accomplished, the vagotomized rats never become completely healthy animals but remain "invalid," the term used by Pavlov<sup>2</sup> in his vivid description of vagotomized dogs.

Both the great difficulties Pavlov encountered in keeping completely vagotomized dogs alive and the identical hazards we observed in rats following such an operation caused us to question the completeness of vagotomy in those clinical studies reporting the operation to be fraught with no serious consequences.

#### SUMMARY

Studies on gastric secretion, motility and nutrition were conducted on more than 200 vagotomized rats. Resection of more than 1 cm. from each vagal trunk was performed below the diaphragm through a left subcostal incision; the upper limit of this resection actually extended into the thoracic cavity for 5 to 10 mm., since the nerves were pulled aborally during the operation.

The immediate effects of vagotomy were studied only in relation to gastric secretion. The interdigestive phase in esophagotomized animals was as completely abolished by bilateral vagotomy during the first twenty-four hours as by large doses of atropine (25 mg. per hundred grams or more). Acute unilateral vagotomy decreased secretion to about one third of normal. Studies on the remote effects of vagotomy were complicated by the fact that none of the vagotomized rats survived more than a week when maintained on a diet of purina checkers.<sup>®</sup> The primary cause of death in these animals was the inadequate digestion of this diet in the stomach and the failure of the stomach to evacuate its contents. Survival was significantly prolonged by the addition of choline hydrochloride to the drinking water (50 to 100 mg. a day per hundred grams of body weight). Yet the animals treated with choline remained in poor condition. Only the use of predigested proteins as a source of nitrogen helped the animals survive as long as seventeen weeks. In the bilaterally vagotomized animals the interdigestive phase of gastric secretion was greatly diminished and sham feeding failed to produce any stimulation. Thus the interdigestive phase of gastric secretion in the rat should be considered mainly a "cephalic phase."



After vagotomy, gastric motility was insufficient to evacuate solids from the stomach. Hair accumulated in tightly packed balls in the antrum at the rate of about 2 cc. every three to four weeks, so that surgical removal became necessary at these intervals. At biopsy or autopsy the esophagus was always greatly distended below the lung root, its diameter being from 5 to 10 mm., as compared with about 2 mm. in normal rats. In most cases the esophagus was filled with food and gastric contents and occasionally with masticated food masses of alkaline reaction. The cardia had the appearance of a fixed incomplete closure. The digestion and absorption of fat and the storage of glycogen by the liver were not noticeably affected by vagotomy during the four week period following the operation.

#### ADDENDUM

Concurrently with our own studies, Harkins and his associates<sup>16</sup> were investigating the effects of vagotomy in rats. From tight ligation of the vagi below the diaphragm, these investigators reported changes in gastric secretion and in ulcer formation in rats in which the pylorus was ligated. Our results recorded in the "acute" vagotomy series are in complete agreement with these.

A summary of our preliminary results was presented in a discussion at the meeting of the American Gastroenterological Society in May 1946 and appeared in *Gastroenterology* in December 1946.<sup>17</sup>

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16. Harkins, H. N.: The Prevention of Pyloric Ligation: Induced Ulcers of the Gastric Rumen of Rats by Transabdominal Vagotomy, *Bull. Johns Hopkins Hosp.* **80**:174, 1947. Harkins, H. N., and Elliott, S. R.: The Influence of Vagotomy on Ulceration of the Gastric Rumen of Rats Following Pyloric Ligation, *Federation Proc.* **6**:1, 1947. Harkins, H. N.; Hooker, D. H.; Alford, C., Jr.; Callander, J.; Elliott, S. R.; Kearns, W., Jr.; Mitchener, J., and Cooley, D. A.: Symposium on Vagotomy for Peptic Ulcer, *Bull. Johns Hopkins Hosp.* **81**:79, 1947. Harkins, H. N., and Hooker, D. H.: Vagotomy for Peptic Ulcer, *Surgery* **22**:239, 1947.

17. Komarov, S. A.: Discussion of Symposium on Peptic Ulcer with Particular Reference to Vagotomy, *Gastroenterology* **7**:620, 1946.

# FIBROSARCOMA, AN UNUSUAL COMPLICATION OF ULCERATIVE COLITIS

Report of a Case

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AND

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NEW YORK

THIS paper reports a rare, malignant complication of ulcerative colitis, namely, fibrosarcoma of the colon. It is becoming increasingly evident, as more statistics are published, that chronic ulcerative colitis in a significant percentage of cases may be complicated by a malignant degeneration of the colon, usually carcinomatous in type.

Lynn,<sup>1</sup> in an extensive review of more than 1,400 cases of ulcerative colitis, found that carcinoma developed in 1.9 per cent of the series. Jackman, Barga and Helmholtz<sup>2</sup> found an incidence of carcinoma of 6.3 per cent in 95 children with ulcerative colitis. Barga, Jackman and Kerr<sup>3</sup> reported an incidence of 3.2 per cent in a group of 871 patients of all ages. In 450 cases of ulcerative colitis at the Lahey Clinic there was an incidence of carcinoma of 2 per cent.<sup>4</sup> Bockus<sup>5</sup> reported an incidence of about 1.5 per cent in 200 cases.

From these figures it is seen that the incidence of carcinoma of the colon in patients of all ages with chronic ulcerative colitis is 1.5 to 3.0 per cent, and this is about doubled when the studies are limited to children.

In 1928 Barga<sup>6</sup> reported 20 cases of a malignant process complicating chronic ulcerative colitis. In 17 it was carcinoma, in 2 lymphosar-

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1. Lynn, D. H.: The Relationship of Chronic Lesions to Carcinoma of the Colon: Chronic Ulcerative Colitis; Collective Review, *Internat. Abstr. Surg.* **81**:269 (Oct.) 1945.

2. Jackman, R. J.; Barga, J. A., and Helmholtz, H. F.: Life Histories of Ninety-Five Children with Chronic Ulcerative Colitis, *Am. J. Dis. Child.* **59**:459 (March) 1940.

3. Barga, J. A.; Jackman, R. J., and Kerr, J. G.: Studies on Life Histories of Patients with Chronic Ulcerative Colitis, *Ann. Int. Med.* **12**:339 (Sept.) 1938.

4. Cattell, R. B., and Boehme, E. J.: The Importance of Malignant Degeneration as a Complication of Chronic Ulcerative Colitis, *Gastroenterology* **8**:695 (June) 1947.

5. Bockus, H. L.: *Gastroenterology*, Philadelphia, W. B. Saunders Company, 1944, vol. 2, p. 593.

6. Barga, J. A.: Chronic Ulcerative Colitis Associated with Malignant Disease, *Arch. Surg.* **17**:561 (Oct.) 1928.

coma and in 1 leukemia. Sarcomatous degeneration of the colon is a much more rare occurrence in cases of ulcerative colitis than is carcinoma. No other figures are available on its incidence, but only an occasional case is encountered. The usual type of sarcoma encountered is lymphosarcoma.

Fibrosarcomas of the large intestine are rare, these being more commonly found in the small intestine. They are usually firm, slowly progressive and fibrous in character. Their growth is more diffuse in character than is the typical carcinoma which tends to be rather localized. Because of this spreading type of growth, fibrosarcomas rarely cause obstruction. Late in their course they have a common tendency to bleed.

#### REPORT OF A CASE

In July 1926, S. R., a married woman then 28 years of age, came under observation for ulcerative colitis. Seven years previously, at 21 years of age, she had undergone a hemorrhoidectomy, which was followed by short periods of diarrhea. This was attributed to an "ulcerated rectum" which had been caused by the operation. For one and a half years before the initial examination, the bouts of diarrhea became more frequent and lasted longer and the stools contained mucus and blood. At the time of examination she had had continuous diarrhea for three months, with a bowel movement every one or two hours accompanied with much tenesmus. She had lost 25 pounds (11.3 Kg.) in the previous year and a half and had been having "chills and fever" at night for a short time before her examination.

Examination revealed a young woman in poor general physical condition. The abdomen was "gassy" and had a poor tone. There was tenderness over the sigmoid region. The rectum revealed generalized proctitis, with superficial ulceration of the mucosa. Moderate anemia was present. Roentgenologic examination showed the stomach to be dilated, elongated and ptosed. The spleen was somewhat enlarged. The cecum was dilated and atonic. There was pronounced evidence of colitis throughout the transverse and descending colon, the sigmoid and the rectum. The colon emptied rapidly. The gastric analysis (Ewald) revealed nothing abnormal. The urine was normal except for a trace of albumin. The feces was fluid and acid. Mucus and blood were present. There was evidence of low starch digestion in the feces and a high fat loss. Culture of the feces revealed a high content of hemolytic coli and a few streptococci.

Because her improvement on medical treatment was only nominal, a cecostomy was performed in 1927 and irrigations were carried out. After this she made a distinct symptomatic improvement. She moved to Los Angeles, where she was treated by various physicians. With daily irrigations of mercurochrome® (merbromin, N. F.) solution and the use of a high protein diet, vitamins and vaccines over several years, her condition improved generally and locally (colon), although she had a recurrence of diarrhea and a reduction in health in 1929. This episode cleared under treatment by Dr. Henry Rooney, of Los Angeles. The cecostomy opening was still patent. Two years later she became pregnant, had a normal gestation and was delivered, and during her pregnancy she was surprisingly free from symptoms. She was not in New York until 1940, when she felt well. Examination revealed a rectovaginal fistula and a rectal stricture which required stretching. She was having only three or four bowel movements

a day. Because the pathologic process in the colon had advanced and because of the aforementioned stricture and fistula, an ileostomy was advised with the intention of subsequently removing the colon and rectum. Operation was refused.

The patient was not seen again until February 1946. At that time she was having considerable free bleeding from the bowel. She had lost 10 pounds (4.5 Kg.) in the preceding four months, was anemic and complained of steady pain in the sigmoid region. With difficulty, because of the rectal stricture, a large mass was felt in the left region of the pelvis and in the lower part of the abdomen. A tentative diagnosis of carcinoma was made, but a roentgenogram revealed an internal blind fistula at the center of the mass. This led to the assumption that the mass was inflammatory about the fistula. Operation was again refused, as the patient was opposed to an abdominal fecal opening.



Fig. 1.—Roentgenogram showing internal fistula extending laterally from fibrosarcoma of the sigmoid.

She was not seen again until August 1947. In the interim of eighteen months she had felt somewhat stronger, but the abdominal pain and rectal bleeding had persisted. During this period an amazing episode occurred. After several days of most intense pain, she delivered through the rectum a mass of tissue "as big as her two fists." The physician called said it was some kind of a "fleshy substance, probably the tumor." There was no pathologic examination. There followed several days of alarming hemorrhage and considerable relief of pain. The patient then thought herself on the road to recovery, especially when the bleeding finally stopped.

In August 1947, when she was seen again, pain and bleeding had returned. Her general health had failed, there was severe anemia and the previously described tumor was palpable in the lower region of the abdomen! Rectal examination again

revealed the tumor, but it seemed somewhat reduced in size. Cystitis was also present. Because of the severe pain, the patient consented to operation.

At operation, performed by Dr. William Hinton, there were dense adhesions between the cecum and the lower part of the small intestine resulting from the

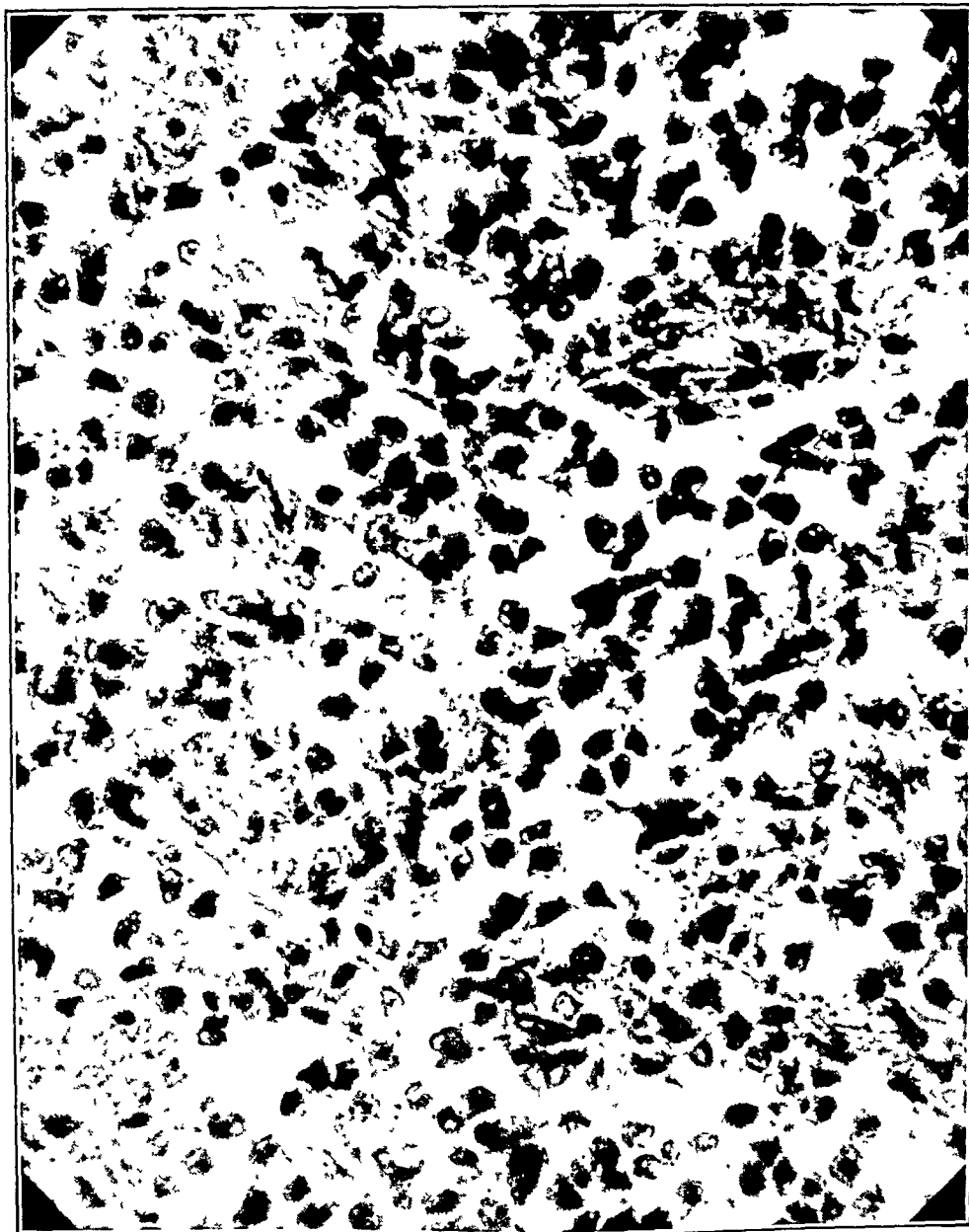


Fig. 2.—Photomicrograph of primary fibrosarcoma of the sigmoid;  $\times 350$ .

previous cecostomy. The distal 10 inches (25.4 cm.) of ileum was definitely diseased, as was the entire colon. A mass was palpable in the lower left region of the abdomen. Ileostomy was performed, the proximal end of the ileum being brought through the lower angle of the wound and the distal end into the upper angle.

After this the pain was slightly relieved, but the bleeding continued. A month later she was reoperated on, the colon and rectum being removed. The entire colon was diseased, and the sigmoid and rectum were markedly involved by what appeared to be a granulomatous process of a stiffened type. It was adherent to the bladder and ovary, and many pelvic lymph nodes were involved. Subsequently, two masses of lymph nodes were removed from both inguinal regions.

The pathologic diagnosis was primary fibrosarcoma of the sigmoid and the upper part of the rectum, with metastatic fibrosarcoma of the ovary and the pelvic lymph nodes. The inguinal lymph nodes had undergone a similar process.

The course was steadily downhill. In about three months after operation, when considerably reduced in weight, the patient died. During the last weeks of life a hard swelling occurred in the right area of the abdomen, no doubt the result of metastasis.

#### COMMENT

A case of chronic ulcerative colitis complicated by the occurrence of colonic fibrosarcoma is reported. The significance of the rôle played by ulcerative colitis in the production of this tumor is uncertain. Fibrosarcoma is a rare tumor of the colon, and its occurrence in the present instance may have been coincidental. On the other hand, carcinomatous degeneration of the colon in chronic ulcerative colitis is well known, and lymphosarcomas have also been reported as complications. It is evident that fibrosarcomatous degeneration of the colon is a most rare complication of chronic ulcerative colitis.

#### SUMMARY

A case of chronic ulcerative colitis occurring in a woman is presented. When she was at the age of 48 years, a malignant process was first noted in the colon. At this time the duration of colitis was twenty-four years. Histologic examination revealed a primary fibrosarcoma of the sigmoid and the upper region of the rectum, with metastatic fibrosarcoma of the ovary and the pelvic and inguinal lymph nodes. The primary lesion was located in only one portion of the bowel, the recto-sigmoid area.

# NEUROFIBROMATOSIS AND PSEUDARTHROSIS

Report of a Case

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SINCE Barber's<sup>1</sup> and Ducroquet's<sup>1b</sup> publications in 1939, bowing of the legs, fractures and pseudarthrosis have been accepted as one of the manifestations of von Recklinghausen's neurofibromatosis. Clinically and roentgenologically the lesions are clearly described, but the morphologic changes taking place in the skeletal system are as yet not completely understood. The first, and apparently only, microscopic examination of tissue in pseudarthrosis connected with neurofibromatosis was published by Green<sup>2</sup> in 1943. The following report of a case of neurofibromatosis also includes the microscopic observations on tissues removed from the area of pseudarthrosis, essentially confirming those described by Green, but in addition it presents unusual features which, to our knowledge, have not been recorded in the past.

## REPORT OF A CASE

B. H., a white girl aged 3 years, 9 months, was admitted to the North Carolina Orthopedic Hospital on Jan. 28, 1947, because of nonunion of fracture of her right tibia. The past history revealed that her development had been normal. The mother noted shortly after birth that one side of the child's genitalia was larger than the other. Little attention, however, had been paid to this until the time of her fracture. The child did not menstruate or masturbate. Recently she had become conscious of herself, refusing to undress in the presence of male members of the family. There were some pigmented areas over her body, present ever since birth. These had not increased in number. No nodules or growth had been noticed on her body. Her appetite had been poor, diet consisting mainly of crackers and soft drinks.

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1. (a) Barber, C. G.: Congenital Bowing and Pseudarthrosis of the Lower Leg: Manifestations of von Recklinghausen's Neurofibromatosis, *Surg., Gynec. & Obst.* **69**:618-626, 1939. (b) Ducroquet, cited by Barber.<sup>1a</sup>

2. Green, W. T., and Rudo, N.: Pseudarthrosis and Neurofibromatosis, *Arch. Surg.* **46**:639-651 (May) 1943.



Fig 1.—Clitoris

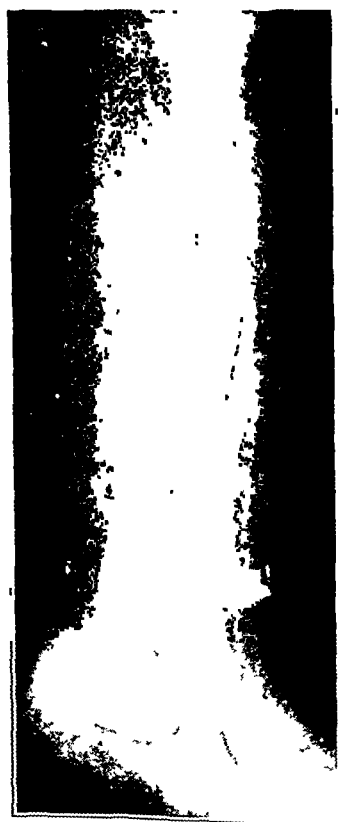


Fig 2.—Pseudarthrosis of tibia and fibula. The bowing of the tibia and erosion of the cortex in its upper one third are readily visible. Also seen is an intra-cortical cyst in the posterior aspect close to and above the fracture of the tibia.



The family history revealed the mother to be 23 years of age, with many pigmented areas on her body for as long as she could remember. The menarche had occurred at the age of 15, and her menstrual history was normal. The father, aged 27 years, had no fractures and no pigmentation or nodular growths on the body. Her maternal grandmother, aged 43, had numerous small nodular growths on the upper part of the chest, neck, face and back. These had been present since the age of 16. Her menstrual history was normal. The maternal grandfather, aged 68, had small nodular growths localized on the trunk. The maternal first cousin sustained a fracture of her tibia at the age of 10. No union occurred. She is now 16 years of age and is unable to walk without the aid of a brace. The patient had no brothers or sisters.

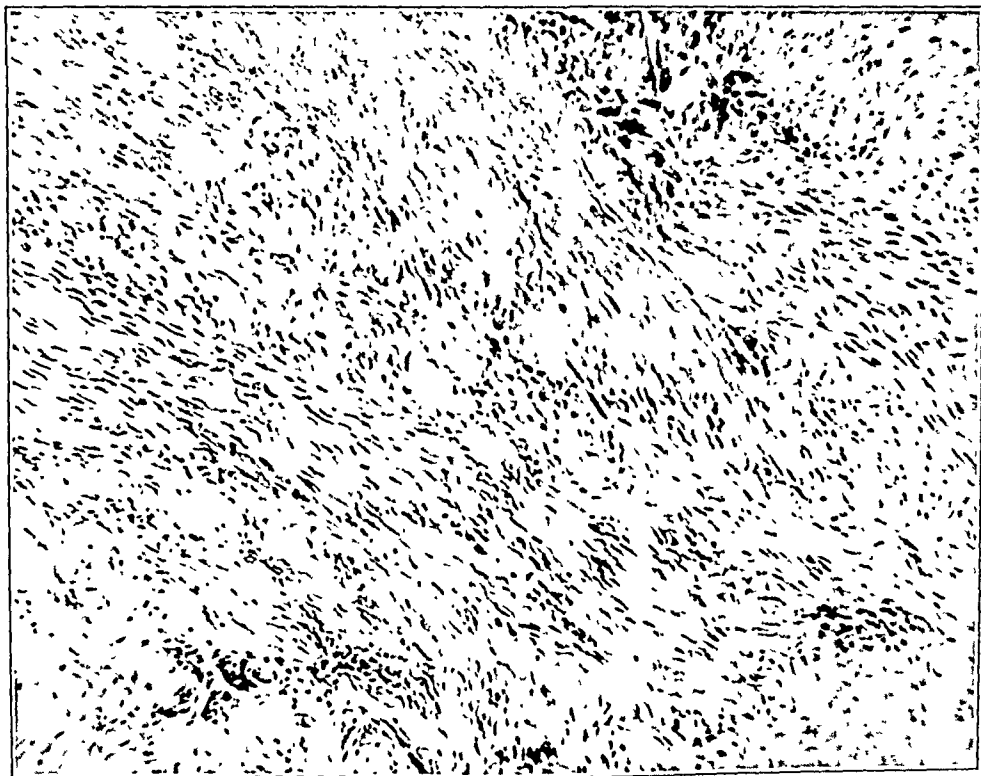


Fig. 3.—Section through the tissue between fracture ends showing streaming of nuclei, palisading and fascicular arrangement.

*Present History.*—The patient fell down four steps, sustaining a fracture of the left tibia, in September 1946. The treatment consisted of reduction of the fracture and application of a plaster cast by an orthopedist. Roentgenologic examination six weeks later failed to reveal any evidence of callus formation. Ten weeks after fracture, the cast was removed, and roentgenologic examination at that time revealed lack of callus formation, with some absorption of bone at the fracture site and spike formation at the distal end of the proximal fragment.

At the time of the patient's admission to the hospital, fifteen weeks after injury, examination revealed a fairly well developed and well nourished blond

girl. She presented café au lait spots on the right side of her thorax and abdomen, their long dimensions running transverse to the body axis. Her clitoris (fig. 1) was greatly enlarged, measuring 4 by 2 cm. There was no pubic hair, and her breasts were infantile. The vagina and the external genitalia were otherwise normal. The left tibia exhibited clinically an ununited fracture in the lower third, with a typical pseudarthrosis (fig. 2).

*Laboratory Findings.*—The Wassermann test gave a negative reaction. A stool specimen was normal, and a vaginal smear was sterile. The urine was normal. The hemoglobin content was 82 per cent, the red blood cells numbered 4,430,000, and white blood cells 7,250, the calcium content was 11.1 mg. per hundred cubic centimeters, the phosphorous 4.7 mg. and alkaline phosphatase 3.7 Bodansky units.

*Course in the Hospital.*—A biopsy was performed on Feb. 24, 1947, and after this a double cortical onlay graft was performed, the right tibia being used as a donor site.

The microscopic examination showed portions of the fractured ends of well formed lamellar bone in continuity with a large mass of connective tissue. The latter enclosed small fragments of necrotic bony spicules and a small area of new formation of bone by direct metaplasia. The main portion of connective tissue was made up of spindle-shaped elements arranged in a parallel and occasionally fascicular fashion, which revealed whorl formation in many areas and at one point distinct palisading of nuclei (fig. 3).

At the time of writing it is only two months since operation, and the final result is undetermined.

#### COMMENT

*A. Changes in Bony Structures and Pseudarthrosis.*—Two, perhaps independent, structural changes were present in the tibia prior to the fracture: first, a cortical erosion with underlying zone of hyperostosis; and, second, an "osteomalacic" process involving the entire tibia, resulting in bowing. The superficial erosion may have been caused by periosteal neurofibromas or by true intraosseous neurofibroma as described by Friedman<sup>3</sup> and others. The "osteomalacic" process, to which many authors refer, would explain the bowing of the long bone and the deformities in other portions of the skeleton but has actually not been demonstrated. Green<sup>2</sup> merely found enlargement of the haversian canals in material from an area of cortical thickening. Brooks and Lehman<sup>4</sup> spoke of increased osteoporosity, but true osteomalacia characterized by destruction of calcified bone and slow replacement by uncalcified osteoid tissue has not been described (Weinmann

3. Friedman, M.: Neurofibromatosis of Bone, Am. J. Roentgenol. **51**:623-630, 1944.

4. Brooks, B., and Lehman, E. P.: The Bone Changes in von Recklinghausen's Neurofibromatosis, Surg., Gynec. & Obst. **37**:587-592, 1924.

and Sicher).<sup>5</sup> The deformities and segmental abnormal growth have hypothetically been ascribed to hyperplastic changes in the lymphatic vessels or to neurinomatous growth in the epiphyseal line (Brooks and Lehman).<sup>4</sup> Moore<sup>6</sup> postulated lack of growth control from neurinomatous changes in the supplying nerve. This assumption is supported by roentgenographic and histologic observations. In a case of neurofibromatosis with localized overgrowth, Moore<sup>6</sup> has clearly demonstrated the absence of horizontal lines of cessation of growth. Although uncontrolled growth may account for the deformities, it does not explain the mechanism of fracture, which in most instances is more or less spontaneous. Kite,<sup>7</sup> explaining the mechanism of fracture, assumed that atrophy and cyst formation cause softening and diminution of the diameter of the shaft, thus allowing the tibia to bend. It is, however, not certain that atrophy actually occurs. The bony architecture may appear rarefied because of defective growth rather than regression. Furthermore, atrophy as well as cyst formation will render the bone frangible rather than flexible. Actual destruction of bone by subperiosteal or intraosseous neurofibromas with so-called subperiosteal cysts must be assumed as the cause of fracture, but further confirmation of this only scantily substantiated hypothesis is needed.

After a fracture has taken place, there is a lack of proper callus formation. Moore<sup>6</sup> assumed that this is likewise due to improper control of bony growth. Since then, however, the actual appearance of neurofibromatous tissue between the fracture ends and the occurrence of intraosseous neurofibroma have been demonstrated (Green<sup>2</sup> and Friedman<sup>3</sup>). Our case may be added to this list. We agree with Green that it is often difficult to distinguish histologically between neurofibroma and nonspecific connective tissue unless nerve fibers can be demonstrated (McNairy and Montgomery<sup>8</sup> and Schlumberger<sup>9</sup>). We have recognized the tissue within the area of pseudarthrosis in our case as neurofibromatous purely on the basis of its dis-

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5. Weinmann, J. P., and Sicher, H.: *Bone and Bones*, St. Louis, C. V. Mosby Company, 1947.

6. Moore, B. H.: Some Orthopaedic Relationships of Neurofibromatosis, *J. Bone & Joint Surg.* **23**:109-140, 1941.

7. Kite, J. H.: Congenital Pseudarthrosis of Tibia and Fibula, *South. M. J.* **34**:1021-1032, 1941.

8. McNairy, J. D., and Montgomery, H.: Cutaneous Tumors of von Recklinghausen's Disease (Neurofibromatosis): Report of Histologic Study, with Special Reference to Nerve Fibers and the Bodian Stain, *Arch. Dermat. & Syph.* **51**:384-390 (June) 1945.

9. Schlumberger, H. G.: Fibrous Dysplasia of Single Bones: Monostotic Fibrous Dysplasia, *Mil. Surgeon* **99**:504-527, 1946.

tinct histologic pattern and because a neurofibromatous nerve was found in the periosteal tissue. Zenker's fixation prohibited silver stain for nerve fibers.<sup>10</sup>

As pointed out by Jaffe,<sup>11</sup> we cannot agree with Thannhauser<sup>12</sup> that whorl formation by itself is pathognomonic of neurofibroma. The palisade arrangement of nuclei, the fascicular arrangement of fibers, the uniformity of the tissue and its connection with a neurinomatous nerve assured us of its neurogenic origin. The correctness of our diagnosis was subsequently verified only by the investigation of other members of the family.

The finding of bone formations, observed in our case, by direct metaplasia from the tumor tissue proper requires consideration. We hold with Jaffe<sup>11</sup> that neurofibroma, in contrast to fibrous dysplasia, does not form bone. It must, therefore, be assumed that the bone spicula was formed in an area where endosteum or periosteum imperceptibly blended into neurofibromatous tissue.

A critical and objective analysis of the histologic interpretation is not only of academic interest. If the pseudarthrosis is purely of connective tissue origin, it would bear out Moore's<sup>6</sup> contention that disturbance of growth is the primary factor. If ingrowth of neurofibroma prevents union, we are dealing with a tumor formation, and treatment should be directed accordingly.

*B. Constitutional Changes.*—A great number of lesions have been added to von Recklinghausen's original one of neurofibromatosis as part and parcel of this disorder. Among these we shall refer only to the endocrine changes and the pigmentation of the skin. Our patient showed a greatly enlarged clitoris and café au lait spots entirely within the level of the skin. Hypertrophy of the clitoris, to our knowl-

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10. After completion of this paper we have had the opportunity of studying tissue removed from the site of the pseudarthrosis in 2 cases of neurofibromatosis with congenital pseudarthrosis. In neither of these was there a histologic pattern as distinctly indicative of neurinomatous growth as that observed in the original case. Massive new growth of young connective tissue in a streaming fascicular fashion was observed, but palisading of nuclei could not be demonstrated. Although not pathognomonic, the histologic observations are compatible with neurofibromatous growth. (The histologic study of the biopsy specimen in these cases was made possible through the courtesy of Dr. Warren White, Greenville, S. C., and Dr. J. H. Kite, Atlanta, Ga.)

11. Jaffe, H. L.: Fibrous Dysplasia of Bone: A Disease Entity and Specifically Not an Expression of Neurofibromatosis, *J. Mt. Sinai Hosp.* **12**:364-381, 1945.

12. Thannhauser, S. J.: Neurofibromatosis (von Recklinghausen) and Osteitis Fibrosa Cystica Localisata et Disseminata (von Recklinghausen): A Study of a Common Pathogenesis of Both Diseases, Differentiation Between Hyperparathyroidism with Generalized Decalcification and Fibrocystic Changes of the Skeleton and Osteitis Fibrosa Cystica Disseminata, *Medicine* **23**:105-149, 1944.

edge, has hitherto been mentioned only twice in connection with neurofibromatosis. In fact, this phenomenon stands in contrast to most previously described manifestations of inner secretory disturbances. Most authors attempt to explain these by pressure of neurofibromas on the glands of inner secretion and the various types of disturbances, resulting mostly in retarded sexual development (Uhlmann and Grossman).<sup>13</sup> Others assume that endarteritis causes changes in the function of glands of inner secretion (Moore<sup>6</sup>). Thannhauser<sup>12</sup> has collected 4 cases from the literature in which there was evidence of precocious puberty and added a fifth case of his own. The classification of this last case, however, as one of neurofibromatosis has not been accepted generally (Jaffe<sup>11</sup>).

Whether the enlargement of the clitoris in our case can be regarded as manifestation of precocious puberty remains questionable. There is the possibility of unrecognized hermaphroditism and that of neurofibromatous change in the clitoris. The latter, however, is not likely, since no cutaneous nodes were demonstrable. On the other hand, the child showed no signs of prematurity. The breasts were those of a child of her age. She did not menstruate, and there was no history of masturbation. The bone age was also in keeping with her stated age. We are thus inclined to register the hypertrophy of the clitoris as another manifestation of neurofibromatosis, perhaps "overgrowth," and not necessarily of sexual precocity.

The café au lait spots cannot be regarded as an absolute criterion of neurofibromatosis if they show no elevation due to beginning changes in the corium. It is the family history in this case that proved the foci of pigmentation to be a manifestation of von Recklinghausen's neurofibromatosis.

*C. Neurofibromatosis Versus Fibrous Dysplasia.*—Thannhauser,<sup>12</sup> on the basis of a detailed analysis of the literature, suggested that neurofibromatosis and fibrous dysplasia (osteitis fibrosa cystica disseminata) are related disorders. He attempted to prove this contention by a collection of case reports from the literature in which both conditions in the same patient were described. The actual morphologic changes underlying the poorly described roentgenologic findings in the skeleton, however, are not mentioned. He stated that café au lait spots are as pathognomonic of neurofibromatosis as the cutaneous nodule itself, although the histologic changes in the skin, as pointed out by Jaffe,<sup>11</sup> are different in the two conditions. He also regarded the whorl formation in fibrous dysplasia as additional evidence of neurofibromatosis. Thannhauser's<sup>12</sup> concept was sharply denounced by Jaffe,<sup>11</sup> and it

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13. Uhlmann, E., and Grossman, A.: Von Recklinghausen's Neurofibromatosis with Bone Manifestations, *Ann. Int. Med.* **41**:225-241, 1940.

has to be admitted that Jaffe's<sup>11</sup> statements seem to bear out his contention that the two disorders are unrelated. The most important points of difference relate to the pattern of osseous lesion and to the hereditary factor. In fibrous dysplasia the lesion occurs primarily within the bone, with new formation of bone spicules. In neurofibromatosis the lesion is situated mostly at the surface, eroding the latter, is rarely within the shaft and never shows new formation of bone. In fibrous dysplasia no familial occurrence is known, while neurofibromatosis is predominantly familial. On the basis of our previous experience with both conditions, Jaffe's<sup>11</sup> depiction must be accepted as clear evidence of the different appearance in the two. The differences outweigh certain resemblances.

The constitutional manifestations in the case we presented were suggestive of osteitis fibrosa cystica. Cutaneous nodules were absent, but café au lait spots and an enlarged clitoris were demonstrated, a combination rarely seen in neurofibromatosis. On the other hand, the family history and the nature of bony changes left no doubt about the true neurofibromatous character of the condition.

The cause of neurofibromatosis or of generalized fibrous dysplasia is not known. Hence, if there are features of resemblance or if cases are reported which present manifestations common to both conditions, it cannot be flatly denied that the entity of generalized fibrous dysplasia may not constitute a subgroup of a general disorder which includes neurofibromatosis. It is true that no hereditary factor has been demonstrated in the relatively small series of cases of generalized fibrous dysplasia, but, conversely, in only 43 per cent of the cases of neurofibromatosis can hereditary tendencies be proved (Uhlmann and Grossman<sup>13</sup>).

The case we presented does not support Thannhauser's<sup>12</sup> concept of the correlation of the two conditions. In spite of certain peculiar aspects, it must be classified as a case of neurofibromatosis. It does, however, demonstrate the confusing character of the so-called constitutional signs and the need for more extensive morphologic examination of the underlying bony lesion.

#### SUMMARY

A case of so-called congenital pseudarthrosis of the tibial bone is presented.

The patient was a member of a family with hereditary von Recklinghausen's neurofibromatosis, and these findings of significance were noted: (a) presence of neurofibromatous tissue between the ends of the fractured bone and (b) constitutional signs, simulating those of osteitis fibrosa cystica, namely café au lait spots and enlarged clitoris.

# EXPERIMENTAL INJURY OF THE COMMON BILE DUCT

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AND

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IT IS DIFFICULT or impossible to determine the incidence of injuries of the hepatic or common bile ducts which occur in the course of operations on the biliary system. Kehr<sup>1</sup> in 1913 reported injury to the common and hepatic ducts fifteen times in one thousand cholecystectomies, or an incidence of 1.5 per cent. Jacobson<sup>2</sup> reviewed the literature up to 1914 and found only 34 cases. Since then, other injuries of this type have been described (Eliot<sup>3</sup> and Eisendrath<sup>4</sup>), but the reviews do not give an accurate idea of the frequency of injury of the common duct since most cases are not reported.

Injuries to the common duct may occur as a result of inflammation of the duct or trauma to the duct. Cole and his associates<sup>5</sup> reported that 76 per cent of a series of strictures were the result of operative injury, Cattell<sup>6</sup> 80 per cent and Walters<sup>7</sup> 90 per cent. In contrast to these, Judd<sup>8</sup> felt that many of the cases attributed to operative trauma were in reality due to ascending cholangitis. As he pointed out, trauma is blamed for many strictures even though the operation thought to be at fault occurred months before. However, not enough is known about the cause of this type of cholangitis for one to duplicate

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1. Kehr, H.: *Die Praxis der Gallenwege-Chirurgie*, München, J. T. Lehmann, 1913, vol. 1, p. 183.

2. Jacobson, J. H.: *Repair and Reconstruction of the Bile Ducts*, Am. J. Obst. **70**:948-965, 1914.

3. Eliot, E.: *The Repair and Reconstruction of the Hepatic and Common Bile Ducts*, Surg., Gynec. & Obst. **26**:81-102, 1918.

4. Eisendrath, D. N.: *Operative Injury of the Common and Hepatic Bile Ducts*, Surg., Gynec. & Obst. **31**:1-18, 1920.

5. Cole, W. H.; Ireneus, C., Jr., and Reynolds, J. T.: *The Use of Vitallium Tubes in Strictures and Absence of the Common Bile Duct*, Ann. Surg. **122**:490-521, 1945.

6. Cattell, R. B.: *Benign Strictures of the Bile Ducts: Causes and Methods of Repair*, S. Clin. North America **23**:701-713, 1943.

7. Walters, W.: *Strictures and Injuries of Bile Ducts: A Study of Results of Operations in Eighty Cases*, J. A. M. A. **113**:209-213 (July 15) 1939.

8. Judd, E. S.: *Stricture of the Common Bile Duct*, Ann. Surg. **84**:404-410, 1926.

it experimentally, and this paper is concerned only with lesions of the common duct produced by direct trauma.

Traumatic lesions of the common duct may be produced in various ways: 1. The duct may be accidentally crushed during an operation. 2. A ligature may be applied to the duct. 3. The duct may be partially or completely cut. 4. A portion of the duct may be accidentally excised. 5. The duct may be cut longitudinally (this is, of course, intentionally done in choledochotomy). 6. The mucous membrane of the duct may be injured by too vigorous probing and scooping. 7. A stone, by long residence in the common duct, may produce injury of the wall of the duct, and it is possible that the passage of a large stone may be followed by mucosal damage.

Eisendrath<sup>4</sup> reviewed the series of Jacobson<sup>2</sup> and that of Eliot<sup>3</sup> in 1920 and also the literature from that date, and he found only 51 cases of injury of the bile ducts due to anatomic variations or errors in technic. The other cases in the literature examined by him involved injuries incident to factors other than errors in technic or anomalies, such as the pathologic changes due to biliary infection.

Since injuries of the duct produced in known ways are not often encountered in man at an optimum time to determine the exact effect of the lesions, the experimental approach has a definite advantage.

#### EXPERIMENTAL PROCEDURE

1. *Operative Technic.*—All operations were performed on dogs under strict surgical asepsis. The abdomen was entered through an incision in the upper midline or right paramedian areas. The lesser curvature of the stomach and the first part of the duodenum were pulled caudad to bring the hepaticoduodenal ligament into view. The external biliary system was then identified and the various procedures carried out. Cotton was ordinarily used for wound closure and silk rarely used.

2. *Anesthesia.*—Morphine and ether intratracheally or a combination of morphine sulfate and pentobarbital was used in all cases. For the morphine-pentobarbital (pentobarbital sodium U. S. P.) anesthesia, 3 mg. of morphine sulfate per kilogram of body weight was given intraperitoneally in 10 cc. of distilled water at least thirty minutes, but preferably sixty minutes, before 50 mg. of pentobarbital per kilogram of body weight was given intraperitoneally or intravenously in 10 cc. of distilled water. Intravenously the barbiturate acted almost immediately and intraperitoneally about five minutes after injection. In rare instances it was necessary to supplement the morphine-pentobarbital anesthesia with up to an additional 20 mg. per kilogram of pentobarbital in distilled water intravenously.

3. *Icterus Index.*—Patency of the bile duct was determined by the presence of excessive bilirubin in the bloodstream. A standard solu-



tion of potassium dichromate was prepared and placed in test tubes in various dilutions.<sup>9</sup> The tubes were sealed, and thus permanent standards, representing 0 to 100 units, were obtained for comparison with unknown serum samples. The colorimetric determinations were done grossly and not in a colorimeter since we were interested only in large increases in the blood bilirubin level.

Because of hemolysis, the icterus index was determined by the method advocated by Harrison.<sup>10</sup> After a clot was allowed to form in the refrigerator overnight, the sample was centrifuged and the serum removed. To 2 cc. of serum an equal amount of acetone was added to precipitate serum albumin and globulin. After spinning down, the supernatant protein-free layer was removed and compared with the color standards and the value obtained multiplied by 2. Of course, some bile is precipitated along with the hemoglobin, but the amount is negligible. The normal by this method is 0 to 8 units.

#### LIGATION OF THE COMMON BILE DUCT

This type of trauma appears often in classifications of causes of stricture of the bile ducts, but as far as reported cases<sup>11</sup> are con-

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9. Kolmer, J. A., and Boerner, F.: *Approved Laboratory Technic*, ed. 4, New York, D. Appleton-Century Company, Inc., 1945, p. 228.

10. Harrison, G. A.: *Chemical Methods in Clinical Methods*, London, J. & A. Churchill, Ltd., 1943, p. 261.

11. (a) Aynesworth, K. H.: Stricture of the Common Bile Duct, *Am. J. Surg.* **28**:562-568, 1935. (b) Behrend, M.: Obliteration of the Common Bile-Duct Following Operation: Cured by an Hepaticoduodenostomy, *Ann. Surg.* **68**:32-33, 1918. (c) Bettman, R. B., and Tannenbaum, W. J.: Complication Arising from Use of Vitallium Tube for Common Duct Repair, *J. A. M. A.* **129**:1165-1166 (Dec. 22) 1945. (d) Colp, R.: Hepatico-Duodenal Intubation with Hepato-Duodenostomy for Traumatic Stricture of the Hepatic Duct. *Surg., Gynec. & Obst.* **80**:190-196, 1945. (e) Douglas, J. D.: Strictures and Operative Injuries of the Bile Ducts, *Ann. Surg.* **84**:392-403, 1926. (f) Erdmann, J. F.: Reconstruction of the Bile-Ducts, *Ann. Surg.* **67**:370-371, 1918. (g) Fowler, W. F.: Reconstruction and Repair of the Hepatic and Common Bile-ducts, *Surg., Gynec. & Obst.* **27**:387-392, 1918. (h) Horsley, J. S., and Horsley, G. W.: Cholecysto-Enterostomy, Choledcho-Enterostomy and Entero-Enterostomy by Means of Rubber Bands: The Use of Rubber Bands in the Mikulicz Operation, *Ann. Surg.* **118**:558-575, 1943. (i) Judd, E. S., and Parker, B. R.: Mortality Following Operations on the Biliary Tract, Pancreas and Liver, *Ann. Surg.* **84**:419-437, 1926. (j) Lilienthal, H.: Injury to the Common Duct, *Ann. Surg.* **67**:619-621, 1918. (k) Mayo, W. J.: Some Remarks on Cases Involving Operative Loss of Continuity of the Common Bile Duct, *Ann. Surg.* **42**:90-96, 1905. (l) McCurrich, H. J.: A New Operation for Restoration of the Common Bile Duct Following Accidental Damage, *Brit. J. Surg.* **31**:304-305, 1944. (m) Migliaccio, A. V.: Reconstruction of Common Duct with Vitallium Tubes, *Am. J. Surg.* **70**:261-267, 1945. (n) Pearse, H. E.: Benign Strictures of the Bile Ducts Treated with a Vitallium Tube, *Surgery* **10**:37-44, 1941. Cole, Ireneus and Reynolds.<sup>5</sup> Eisen-drath.<sup>4</sup> Eliot.<sup>3</sup> Jacobson.<sup>2</sup> Kehr.<sup>1</sup>

cerned, actual simple encirclement of the common bile or common hepatic duct with a ligature and the duct left uncut is not common (see table). In the other cases having to do with ligation, only part of the wall of the duct was included in the ligature or a knuckle of the duct was tied as observed by Phemister<sup>12</sup> or the duct was clamped, ligated and cut. In the last case, obstructive symptoms and signs develop while the ligature holds, and when it gives way, external biliary fistula occurs. Allen<sup>13</sup> has removed chronic surgical gut ligatures from the end of a common duct severed at operation a month earlier. In accidents such as the one just described, ligation is of secondary importance in production of the injury since the main source of trauma

*Reported Cases of Simple Ligation of Common Duct*

Lillenthal, H.....	Cholecystectomy	Hepatic duct mistaken for cystic duct and ligated	Found at necropsy
Bottomley, J. T.....	Cholecystectomy	Common hepatic duct almost completely occluded by ligature about cystic duct and artery	Ligature removed at secondary operation and patient recovered
Phemister, D. B.....	Cholecystectomy	Knuckle of hepatic duct included in ligature controlling cystic artery hemorrhage	Fistula formed
Eisendrath, D. N.....	Cholecystectomy	Part of hepatic duct ligated controlling cystic artery hemorrhage	No stricture
Russell, T. H.....	Cholecystectomy	Complete ligation of common duct	Ligature removed at secondary operation; T tube which was inserted pulled out and was followed by stricture
Brewer, G. E. (personal communication to Eliot <sup>3</sup> )	Cholecystectomy	Partial ligation of the common hepatic duct	Healed without occlusion
Russo, C.....	Cholecystectomy	Mass ligation of the common duct	Found at necropsy
Douglas, J.....	Cholecystectomy	Clamp and suture ligature to control bleeding	Fistula formed

is the improper application of forceps, resulting in cutting or resection of the duct. From the tabulation it is apparent that when a portion of the duct was ligated the wall under the ligature was deprived of its blood supply and sloughed, allowing bile to pour into the abdominal cavity, or, contrastingly, healed without occluding the ductal lumen. Of the 3 cases in which a loop of ligature was placed around the duct and the duct left intact, 1 was found at autopsy<sup>14</sup> and the other 2 at secondary

12. Phemister, D. B.: Reconstruction of the Hepatic Duct, *Surg. Clinics*, Chicago **1**:553-560, 1917.

13. Allen, A. W.: A Method of Re-Establishing Continuity Between the Bile Ducts and the Gastro-Intestinal Tract, *Ann. Surg.* **121**:412-424, 1945.

14. Russo, C.: Five Years of Gall Bladder Surgery in a General Hospital: A Review of Three Hundred and Thirty-Seven Consecutive Gall Bladder Operations. *Am. J. Surg.* **58**:388-397, 1942.

operation for biliary obstruction. Bottomley's patient<sup>15</sup> recovered when the ligature was cut at reoperation. Russell<sup>16</sup> cut the ligature but also did a choledochotomy with a T tube drainage at secondary operation. The tube was removed, and a month later he reoperated for obstruction and found a stenosis of the duct 1 inch (2.5 cm.) long at the site of choledochostomy. The literature reviewed did not contain a report of a case in which the duct was ligated, the ligature cut at a second operation and stricture formed.

In studies on the effect of operations on the gallbladder, McWhorter<sup>17</sup> ligated the cystic duct of 7 dogs with plain fine surgical gut, and the latter was absorbed in ten to fourteen days without stricture or scarring of the duct over a period of one week to four months. In 5 animals the cystic duct, ligated with surgical gut, failed to reopen. Two of these ducts reopened after only seven postoperative days, but the other three were found occluded at the end of one to five months. According to this observer, the duct becomes patent unless unnecessary trauma or heavy suture material is used, and he suggested that "temporary ligation of the bile ducts with fine catgut may aid in controlling hemorrhage, especially about the cystic duct, and in the diversion of bile."

*Experimental Data.*—The common bile ducts of 10 dogs were ligated and the ligatures left in place for varying periods to observe the effect of this type of trauma on the bile ducts. The ducts of 8 of these animals were tied with cotton. This nonabsorbable ligature was removed successfully, unsuccessfully or not at all, as the case may be, in a given period. In 2 dogs the duct was tied with different sizes of plain surgical gut and left permanently.

#### CONDENSED PROTOCOLS

1. In dog 23 the common bile duct was tied with white cotton on April 1, 1947. The icterus index was 12 units on the second postoperative day, 16 units on the third day and 30 units on the fourth day. On April 10 an attempt was made to remove the ligature from the duct, but the wall of the duct gave way and the animal died.

2. In dog 47 the common duct was ligated with cotton on March 8, 1947. The icterus index was 100 units on March 10, and the ligature was successfully removed. The dog recovered and no pathologic change was seen in the duct at necropsy on July 15, 1947.

3. In dog 49 the common bile duct was ligated with black cotton on Oct. 10, 1946. The icterus index rose to 50 units on October 13 and 100 units on October 16, remained elevated for a time and returned to normal. Necropsy on December 14

15. Bottomley, J. T.: Personal communication to Eisendrath.<sup>4</sup>

16. Russell, T. H.: Reconstruction of Common Bile Duct: Seven Year Result, *Ann. Surg.* **111**:145-147, 1940.

17. McWhorter, G. L.: Clinical and Experimental Operations on the Gallbladder and Common Duct: Results of Primary Suture, *Arch. Surg.* **35**:1099-1125 (Dec.) 1937.

showed dilated gallbladder and ducts down to the ligature, normal below this, and bile in the duodenum.

4. In dog 51 the common duct was ligated with white cotton on Oct. 10, 1946. Two days later the icterus index was 100 units, and it remained elevated until October 27, when it was found normal. The icterus index was repeatedly normal after this. At reoperation on December 12 the common duct was found to be patent though larger than normal, and no ligature could be seen.

5. In dog 81 the common bile duct was ligated with cotton on March 18, 1947. On March 20 the icterus index was 20 units and the ligature was removed. The gallbladder and duct were dilated and the animal made an uneventful recovery. Necropsy was performed on April 21, 1947. Bile was found in the duodenum and the common bile duct was patent though slightly dilated above the site of the old ligature.

6. In dog 82 cholecystectomy was performed; the common bile duct was ligated twice with cotton on Jan. 17, 1947. On Jan. 21 the icterus index was 100 units, and it remained elevated. At reoperation on January 24 to remove the ligature the wall of the tremendously dilated proximal duct was nicked accidentally and the dog died.

7. In dog 97 the common duct was ligated with cotton on March 20, 1947. On March 22 the icterus index was 8 units and the ligature was removed. The gallbladder was six times the normal size and the common duct the size of a lead pencil. The dog recovered. At necropsy on April 23 the duct appeared normal.

8. In dog 110 the common bile duct was ligated with no. VIII cotton on April 3, 1947. The icterus index was 6 units on April 5, 12 units on April 6 and 40 units on April 10, and it remained elevated. On May 17 the duct perforated during an attempt to remove the ligature, but the animal recovered. Necropsy was performed on July 10. The common duct was intact and patent.

9. In dog 187 the common bile duct was ligated with no. II plain surgical gut on June 7, 1947. On June 12 the icterus index was 14 units, on June 18, 27 units and on June 25, 0 units. At necropsy on July 18 the common duct was larger than usual but patent.

10. In dog 188 the common bile duct was ligated with no. III plain surgical gut on June 14, 1947. The icterus index was 20 units on June 18, 4 units on June 25 and 6 units on June 27. At necropsy the common duct was enlarged but stricture was not apparent. There was bile in the duodenum.

*Summary and Conclusions.*—1. Heavy plain surgical gut placed about the common ducts of 2 dogs was absorbed, and the biliary obstruction was relieved. 2. A nonabsorbable ligature on the common duct can be removed after several days, and the animal will recover. Stricture did not develop subsequently during the period of observation. In dog 41 the ligature was definitely in place ten days before slipping without producing a stricture. In another animal, dog 49, the duct was patent proximal and distal to the ligature, which had slipped a little, allowing bile to pass into the duodenum sixty-nine days after operation. 3. When trying to remove a ligature from the duct at secondary operation, care must be exercised to avoid pulling the ligature too hard. 4. Among 2 dogs injured in this way, healing occurred in 1, dog 110, and that without stricture.

## CRUSHING OF THE DUCT

This is another type of trauma frequently noted in classifications of injury of the bile duct. Surprisingly, there are few case reports in the literature from which one could assume that the actual trauma of clamping has been responsible for injury to one of the bile ducts. Pearse<sup>11a</sup> reported a case in which the upper part of the common duct was clamped while controlling hemorrhage from the cystic artery and the clamp left on. It is questionable whether the ultimate stricture was due to this or to choledochotomy performed at secondary operation. When the majority of case reports speak of "clamping of the duct," the act of clamping is followed usually by ligation and cutting or by ligation alone of a portion of the duct.

*Experimental Data.*—The common ducts of 5 dogs were crushed for varying lengths of time with large Ochsner forceps.

## CONDENSED PROTOCOLS

1. In dog 10 the common duct was crushed for ten minutes with large Ochsner forceps on Nov. 14, 1946. Recovery up to November 22 was uneventful. On this date evisceration occurred, and reclosure was attempted but the dog died. At necropsy the common duct appeared thicker than normal and slightly dilated. There was no sign of obstruction.

2. In dog 30 the common bile duct was clamped with Ochsner forceps for five minutes on Feb. 27, 1947. The icterus index remained normal, and necropsy, on July 2, 1947, revealed a normal duct.

3. In dog 85 the common duct was crushed for ten minutes with large Ochsner forceps on March 11, 1947. Recovery was uneventful. The icterus index was repeatedly normal until death occurred on April 27 from distemper. At necropsy the gallbladder was three times normal size and the common duct a little larger than normal.

4. In dog 48 the duct was crushed for ten minutes on March 11, 1947, with a large Ochsner forceps. The icterus index remained normal, and the animal was killed on April 30. At necropsy the gallbladder was normal. The common bile duct was possibly a little dilated.

5. In dog 11 the common duct was crushed for ten minutes on Nov. 14, 1946. There was a normal icterus index, but the animal died on November 22 of distemper.

*Summary and Conclusions.*—No jaundice was noted in 5 dogs after the ducts were crushed for ten minutes with an Ochsner forceps, but in about half the animals there was dilatation of the ducts.

## CUTTING OF THE DUCT

Statements regarding the regenerative properties of the bile ducts have appeared from time to time. Sullivan<sup>18</sup> stated that he cut the common duct in the hepaticoduodenal ligament experimentally and that

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18. Sullivan, A. G.: Reconstruction of Bile Ducts, J. A. M. A. **53**:774-777 (Sept. 4) 1909.

invariably it healed without anything further being done. Others have commented on the remarkable regenerative powers of the duct,<sup>19</sup> and ducts reconstructed experimentally<sup>20</sup> and clinically<sup>21</sup> eventually became lined by the epithelium of the bile duct mucosa.

Cutting is frequently a cause of injury to the bile passages. Fortunately, injuries to the duct in this manner are fairly often recognized at primary operation and the damage repaired at that time. Stricture has been reported after such repairs.

*Experimental Data.*—To observe this phenomenon, the common ducts of several dogs were simply severed, or a section was removed, or the duct was hemisectioned or a section was removed and the cut ends anastomosed.

#### CONDENSED PROTOCOLS

1. In dog 30 a 2 cm. portion of the common duct was removed and the cut ends left free in the hepaticoduodenal ligament on Oct. 22, 1946. There was a gradual rise in the icterus index to 100 units on November 4. At necropsy the cut ends of the duct were isolated by a mass of fibrous tissue. There were no signs of anastomosis or regeneration.

2. In dog 142 removal of 1 cm. of the common duct and anastomosis of the cut ends with fine silk were accomplished on April 9, 1947. Recovery up to April 20 was uneventful and then jaundice developed, and the animal was found dead on April 27. At necropsy leakage at the site of anastomosis was seen.

3. In dog 72 the duct was cut in the hepaticoduodenal ligament on Feb. 27, 1947. The icterus index was 100 units on March 4, 1947. The dog was found dead on March 7. At necropsy there was bile in the peritoneal cavity. No anastomosis was seen.

4. In dog 42 the common duct was cut in the hepaticoduodenal ligament on Jan. 10, 1947. The icterus index was 0 units on January 10 and 18. On January 21 it was 21 units, and on January 30 it was 30 units. Deepening jaundice appeared, and the dog died on March 4. At necropsy the gallbladder and biliary tree were enormously dilated. The distal portion of the common duct was found to end near the greatly dilated portion of the proximal segment of the common duct, but no continuity could be demonstrated between the two.

5. In dog 150 the common duct was cut in the hepaticoduodenal ligament on March 8, 1947. On March 10 the icterus index was 20 units, and it increased thereafter to 100 plus. Jaundice became intense. The dog died on April 2. At necropsy there was bile in the peritoneal cavity. The cut ends of the common duct were separated 1.5 cm. The distal duct was normal in appearance. The proximal duct was dilated three times normal. There was no anastomosis.

6. In dog 160 the common duct was cut half-way through with scissors on March 15, 1947. The icterus index remained normal. The dog was killed on June 6. At necropsy the common bile duct appeared normal.

19. Eliot, E.: Benign Cicatricial Strictures of the Bile Ducts, *Ann. Surg.* 104:668-701, 1936. Jacobson.<sup>2</sup>

20. Danis, R., cited by Jacobson.<sup>2</sup> Sullivan.<sup>18</sup>

21. Jenckel, cited by Jacobson.<sup>2</sup> Roeder, C. A.: Transplantation of a Biliary Fistulous Tract Into the Duodenum, *Ann. Surg.* 91:144-147, 1930.

7. In dog 111 the common duct was hemisectioned on March 15, 1947. There was no rise in the icterus index. The dog was killed on April 16. At necropsy the duct appeared normal.

*Summary and Conclusions.*—1. The severed common bile ducts of 3 dogs failed to anastomose or regenerate after nine, twenty-six and fifty-four days respectively. 2. A 2 cm. section of common duct was removed from 1 dog, but no anastomosis occurred in forty-six days. 3. A 1 cm. piece of common duct was removed from another dog and the ends anastomosed, and partial union occurred in eighteen days. 4. The common duct was hemisectioned in 2 dogs and healed perfectly without obstruction. 5. In view of these observations on healing together with those noted after choledochotomy (ulceration of the duct) and severance of the duct while removing a ligature, it would seem that healing of the common duct, in the dog at least, is not as remarkable as is perhaps generally believed and that healing is best promoted, as elsewhere, by contiguity of cut surfaces.

#### ULCERATION OF THE COMMON BILE DUCT

A method could not be devised which would include all the factors present during ulceration of the duct by an impacted stone. A procedure was employed, however, which destroyed the mucosa and perhaps some of the underlying layers, to reproduce the actual destruction of the mucosa by stone and to equal, in intensity at least, the trauma produced by too violent scooping or probing of the duct during choledochotomy.

*Experimental Data.*—Choledochotomy was performed on 2 dogs. The wall of the common duct was cauterized by a crystal of phenol and the effect neutralized with alcohol when whiteness persisted for at least thirty seconds and left open.

#### CONDENSED PROTOCOLS

1. In dog 143 the common bile duct was opened and a phenol crystal touched to the wall until the mucosa turned white (about thirty seconds). The crystal was removed and 10 per cent alcohol sprayed on the wall. The opening in the ductal wall was not sutured. The icterus index was normal on April 3 and 4 but 100 units on April 10. The dog died on April 24. At necropsy there was leakage from the choledochotomy wound.

2. In dog 87 the common duct was traumatized with phenol. The postoperative recovery was uncomplicated. The icterus index was normal, and the dog was killed on May 1. At necropsy the gallbladder was somewhat larger than normal. The common bile duct was healed and showed no sign of stricture or other deformity.

*Summary and Conclusions.*—Destruction of an area of common duct mucosa by phenol may interfere with healing of the duct, but stricture had not formed after twenty-one days in 1 dog.

SUMMARY

1. A surgical gut ligature on the common bile duct was absorbed and the jaundice cleared.

2. A nonabsorbable ligature can be removed, with relief of the obstruction. Stricture did not follow during the period of observation.

3. Crushing of the common bile duct may be followed by dilatation of the duct, but jaundice did not develop.

4. Complete section of the common duct was not followed by spontaneous healing of the duct. Partial section of the duct, or partial anastomosis after complete section, is usually followed by healing of the duct.

5. Choledochotomy and cauterization of the duct with phenol may or may not be followed by healing of the duct.



## INTUSSUSCEPTION DUE TO FAMILIAL ADENOMA OF THE SMALL INTESTINE

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AMONG the surgical emergencies of the abdomen, intussusception is one of the most urgent, and the relative infrequency of this condition after infancy makes isolated cases in older persons of particular interest to the general surgeon.

Intussusception in the first two years of life is of fairly frequent occurrence, while in the rest of the life span it is peculiarly infrequent. In an analysis of cases of intussusception, Perrin and Lindsay<sup>1</sup> found that of 400, 78.5 per cent occurred in the first two years and 69.75 per cent in the first year of life. Of the type of intussusception occurring in infants, no etiologic factor was apparent in 95 per cent of the cases, while in the form found later in life a definite causative agent usually is found. Dickson<sup>2</sup> stated that intussusception in the adult is always secondary to some underlying condition.

Perrin and Lindsay listed the following causes of intussusception: (1) perverted peristalsis, with retrograde movement of one segment of bowel on another; (2) a paralytic condition of the intestine, allowing prolapse of one portion into another, and (3) the presence of some congenital abnormality, such as a constriction, or some growth, such as carcinoma, acting as the exciting cause. In cases of intussusception in infants in which no obvious mechanism is found, the condition probably is due to perverted peristalsis, paralysis of a segment of the intestine or a congenital constriction ring, or, possibly, as Watts<sup>3</sup> pointed out, it may result from congenital hypermotility of the cecum, allowing ileocolic intussusception to develop. Of the type found after the first two years of life, by far the commonest cause is the presence of a tumor in the bowel.

Tumors of the small bowel have given rise to a considerable amount of writing in recent years, chiefly because of their relative rarity.

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From the Surgical Service of Stuart Circle Hospital.

1. Perrin, W. S., and Lindsay, E. C.: Intussusception, *Brit. J. Surg.* **9**:46, 1921.

2. Dickson, W. B.: Multiple Adenomas of the Jejunum, *Ann. Surg.* **119**:283, 1944.

3. Watts, L. H.: Intussusception in the Adult, *Ann. Surg.* **53**:408, 1911.

Usually their presence is discovered only when some complication of their existence has taken place. The commonest causes of their discovery are intussusception, obstruction of the lumen from increasing growth and malignant degeneration. Rankin and Newell,<sup>4</sup> after a survey of benign tumors of the small intestine at the Mayo Clinic, remarked on the rarity of these tumors. Raiford<sup>5</sup> listed as causes of the relative infrequency of tumors in the small bowel (1) the relative freedom from stasis of the small intestine (except in the terminal portion of the ileum, where the incidence of tumors is highest) and (2) the fact that there is little chance for arrested development and misplaced embryonal tissue in the small intestine because it develops chiefly during the last four months of fetal life. Raiford could find only 50 benign tumors of the small intestine in the material of 11,500 autopsies and in 45,000 surgical pathologic specimens at the Johns Hopkins Hospital, and Rankin and Newell reported only 35 cases from the records of the Mayo Clinic.

Pathologically, benign tumors of the small intestine may arise from any of the cells normally present in the intestinal wall. Thus there may be adenomas, fibromas, lipomas, angiomas and myomas. These tumors may be sessile, pedunculated or in the intestinal wall, and all pedunculated tumors may be classified as polyps. The commonest benign tumor of the small bowel is the adenoma. Raiford found 15 adenomas in a series of 50 benign tumors, while at the Mayo Clinic there were 11 adenomas in a series of 35 benign tumors. Willis,<sup>6</sup> however, emphasized the rarity of adenomas, and he found only 19 cases in a series of 7,592 autopsies at the Massachusetts General and Boston City Hospitals up to 1920. Adenomas of the small intestine may occur at any age and in either sex, and they are found oftenest in the lower portion of the small intestine. They are usually single but may be multiple, and they may be sessile or pedunculated. Polyposis is not uncommon in the colon and may be seen in the ileum, and multiple adenomas in the small intestine have been described by Dickson,<sup>2</sup> Brown<sup>7</sup> and Wardill.<sup>8</sup> The tumors vary in size from a few millimeters to a few centimeters in diameter. Section often shows a papillomatous structure with a white pedicle and fibrous tissue permeating the growth and dividing it into

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4. Rankin, F. W., and Newell, C. E.: Benign Tumors of the Small Intestine, Surg., Gynec. & Obst. **57**:501, 1933.

5. Raiford, T. S.: Tumors of the Small Intestine, Arch. Surg. **25**:122 (July); 321 (Aug.) 1932.

6. Willis, A. M.: Intussusception Resulting from Benign Tumor of the Intestine, Surg., Gynec. & Obst. **30**:603, 1920.

7. Brown, R.: Invagination Ileus in Polyposis of Small Intestine, Arch. Surg. **15**:441 (Sept. 27) 1927.

8. Wardill, W. E. M.: Polypi in the Bowel Causing Intussusception, Brit. J. Surg. **13**:158, 1925.

lobules. The cells have the appearance of those of the intestinal mucosa, but undifferentiation and rapidity of growth are often present at the periphery. The incidence of malignant growths was found by Raiford to be 6.6 per cent, but Doering stated that 45 to 50 per cent of adenomas undergo malignant changes. The vast majority exhibit the uniform glandular structure of the mucosa of the small intestine. The presence of inflammatory cells in the periphery and the association of adenomas with pinworm infection and with colitis have suggested that an inflammatory mechanism is responsible for the development of these tumors, while another theory is that they arise from cell rests or other defects in the mucosa. The symptoms of adenoma of the small intestine are usually those of bleeding or obstruction, and recurring intussusception due to tumor may be the cause of irregular attacks of colicky abdominal pain in adults without obvious cause (Oughterson and Cheever).<sup>9</sup> Polyposis of the small intestine clinically may resemble colitis.

The incidence of intussusception associated with tumors of the small bowel is much greater with benign than with malignant growths. Intussusception was reported by Raiford to have occurred in 23 per cent of his cases, while Rankin and Newell found it in 33 per cent of their series. Staemmler and Joyce<sup>10</sup> both listed an incidence of 30 per cent.

Intussusception as a complication of adenoma of the small intestine has been reported rather frequently in the past thirty years (Brown,<sup>7</sup> Fiske,<sup>11</sup> Cave,<sup>12</sup> Cassidy and Macchia<sup>13</sup> and King<sup>14</sup>). The mechanism of intussusception due to tumor has been well described by Wardill.<sup>8</sup> He postulated two distinct processes: 1. When the tumor is pedunculated, it may be seized by the peristaltic wave and dragged along through the lumen of the bowel, pulling a segment of intestine behind it and causing invagination, with the tumor at the apex of the intussusceptum. 2. The tumor may act as a foreign body and produce a spasmodic contraction of the intestine around it, with inhibition of the part distal to it; "the conditions are now favorable for that act of peristaltic gymnastics whereby the contracted part is induced to slip into the dilated portion," producing intussusception with the tumor elsewhere than at the apex of the intussusceptum.

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9. Oughterson, A. W., and Cheever, D.: Recurring Intussusception Caused by Intestinal Neoplasms, Requiring Multiple Operations for Its Relief, *Surg., Gynec. & Obst.* **48**:682, 1929.

10. Joyce, T. M.: Tumors of the Small Intestine, *Ann. Surg.* **100**:949, 1934.

11. Fiske, F. A.: Intussusception Due to Intestinal Tumors, *Ann. Surg.* **106**:221, 1937.

12. Cave, H. W.: Tumors of the Small Intestine, *Ann. Surg.* **96**:269, 1932.

13. Cassidy, J. M., and Macchia, B. J.: Polyposis of Duodenum and Jejunum: Report of an Instance, *Am. J. Digest. Dis.* **1**:755, 1934.

14. King, E. L.: Benign Tumors of the Intestines, *Surg., Gynec. & Obst.* **25**:54, 1917.

The familial tendency of polyposis of the bowel has been pointed out by Horsley and Keasbey,<sup>15</sup> by Bockus,<sup>16</sup> by Huchtemann,<sup>17</sup> and by Junglung.<sup>18</sup> More specifically, the occurrence of tumors of the small intestine in more than one member of a family has been cited by Gatersleben<sup>19</sup> and others.

The occurrence in more than one member of a family of intussusception of the small intestine due to adenoma is rare and particularly interesting. The cases reported here are instances of this sort.

#### REPORT OF CASES

CASE 1.—*First Admission* (quoted from Willis<sup>6</sup>).—"A. K., female, aged 7, admitted to Johnston-Willis Sanatorium on April 6, 1919. The family history is negative. One year prior to admission, the patient had an attack of abdominal pain of great severity, but recovered without being seen by any physician. Three weeks ago, a similar attack occurred, lasting several hours. Again, no physician was called. Three hours before admission, while playing in park, the patient was seized with agonizing abdominal pain, accompanied by nausea and vomiting. The pain was so severe that the child was completely prostrated. Physical examination showed a mass, several inches in diameter and about a foot in length, extending diagonally across the abdomen, just above the umbilicus. A diagnosis of intussusception was made.

"Two hours after admission, the condition being unaltered, operation was advised. Through a midline incision, the mass was delivered and found to consist of an ileal intussusception about two feet in length. [This was found at a later operation to have been jejunal.] The invagination was reduced with great difficulty and . . . a small pedunculated tumor was found at its apex. The serosa over the attachment of the tumor presented a puckered appearance, resembling that sometimes seen in the skin over early carcinoma of the breast. For this reason, it was deemed wise to resect about 6 inches of the small intestine, followed by end-to-end anastomosis. The child was reported fully recovered 8 months after operation.

"*Pathological Report.*—The tumor measured 2 centimeters in length, 1 centimeter in thickness, and 1 centimeter in depth. It was soft, smooth, and pinkish-gray in color, and it was attached to a small portion of the bowel wall by a pedicle which measured one-half centimeter in length and one-half centimeter in thickness. On section it appeared to be lobulated and the lobules varied in size from a pin-point to a pin-head. Microscopic section (transverse) showed the tumor to have gland-like structure, not unlike that seen in normal mucosa. The acini were lined by a columnar epithelium and goblet cells. Some of the acini were cystic and contained mucus. There was a connective-tissue stroma between the gland-like collections of epithelium. Near the pedicle and in the region of its attachment to the bowel wall the acini suggested a malignant degeneration, but there was no apparent invasion of the bowel wall. Diagnosis: adenoma."

15. Horsley, J. S., and Keasbey, L. E.: Tumors of the Small Intestine, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1943, vol. 6, chap. 17.

16. Bockus, H. L.: Gastro-Enterology, Philadelphia, W. B. Saunders Company, 1943, vol. 2, p. 128.

17. Huchtemann, cited by Roan.<sup>21</sup>

18. Junglung, O., cited by Roan.<sup>21</sup>

19. Gatersleben, H., cited by Horsley and Keasbey.<sup>15</sup>

*Second Admission.*—Eighteen years later, on Nov. 2, 1935, A. K., then 25 years old, was admitted to St. Luke's Hospital, complaining of abdominal pain. She had noticed slight pain in the abdomen on the night of November 1, and at 6 a. m. on November 2 she was seized with severe midabdominal pain, which grew steadily worse until the time of admission. There had been no nausea or vomiting. One year previously, she had experienced a similar attack, lasting three days. The past history revealed that the patient had had an intussusception caused by an adenoma in 1919 (see foregoing account). In 1928 she had been hospitalized at the Sheltering Arms Hospital with the diagnoses of chorea, rheumatic endocarditis (mitral) and secondary anemia, and she had received transfusions for anemia. She had been under observation for several years for an unexplained "secondary" anemia, and her hemoglobin reading had fluctuated between 35 and 75 per cent after treatment with iron. She also gave a history of chronic fatigue and had been told by her family that she was lazy.

*Physical Examination.*—On admission the patient was acutely ill and in obvious pain, with an initial temperature of 96.4 F., a pulse rate of 82 and a respiratory rate of 16. The heart was slightly enlarged to the left, and there was a soft systolic murmur at the apex transmitted up along the left border of the sternum, but the rhythm and rate were normal. The abdomen was tense and rigid, with tenderness throughout. No mass was palpable. The urine showed a trace of albumin and gave a 3 plus reaction for acetone. The red blood cell count was 3,900,000, with 51 per cent hemoglobin, and the white blood cell count 13,100, with 90 per cent polymorphonuclear leukocytes and 10 per cent lymphocytes. The preoperative impression was that of intestinal obstruction.

*Operations.*—On November 2, a midline incision was made through the old scar. The colon and appendix were normal. In the left lower portion of the abdomen there was a tremendously distended loop of small bowel which had been invaginated. Just outside this mass there was a scar on the small bowel, which evidently indicated the site of the previous resection. This scar was not adherent, and the lumen was normal. The small bowel was easily reduced, and near the head of the invaginated bowel a tumor, apparently a polyp, about 1½ inches (3.8 cm.) in diameter, was found in the lumen. This tumor did not completely obstruct the bowel. On account of the edema and the fact that the obstruction had been complete for more than twenty-four hours, it was considered wise to postpone resection of this area until the patient had recovered from the obstruction and the bowel had been restored to normal. The wound was therefore closed with sutures of chromic surgical gut U.S.P., silkworm gut and silk.

On November 11, an incision was made in the midline, with excision of the old scar. The entire small bowel was explored. It was normal except for moderate edema in the area which had previously been strangulated. The polyp was again intussuscepted for a distance of about 6 inches (15 cm.), evidently because of the contraction brought on by the spinal anesthesia. The polyp was the only such tumor found in the entire length of the small bowel, and it was attached by a long pedicle. It could be moved freely up and down the bowel for a distance of about 2 inches (5 cm.) on each side. The bowel was opened immediately over the polyp by a transverse incision. The segment of the bowel was excised close to the mesenteric border, to which the pedicle was attached, and the wound closed with continuous sutures of chromic surgical gut and interrupted mattress sutures of fine silk. This point in the bowel was about 3 feet (90 cm.) from the duodeno-jejunal junction and about 6 inches (15 cm.) from the site of the former resection. The appendix was removed. The wound was closed with sutures of chromic surgical gut U.S.P., silkworm gut and silk.

*Pathologic Report.*—The polyp measured 3 by 3 by 2 cm., and had a cauliflower-like, thick, short pedicle. The growth did not invade the deeper layers of the intestinal wall. Microscopic examination showed it to be made up of intestinal glands of various sizes and in orderly arrangement. The epithelial cells surrounding the glands showed no invasive tendency. The tumor was diagnosed as a benign papilloma of the intestine.

*Progress.*—Recovery from the operations was uneventful, and the patient has since been perfectly well.

CASE 2.—W. G. B. Jr., the 4 year old son of the patient in case 1, was admitted to Stuart Circle Hospital at 2:30 p. m. on March 16, 1947. The child's mother stated that he had awakened at 4 a. m. on the day prior to admission, complaining of severe abdominal pain. Nausea and vomiting followed shortly thereafter, and the pain, although intermittent, continued all that day and night and was present at the time of admission on the following day. Since the onset of the pain, the child had had no bowel movement. Enemas were returned clear without gas, and no blood had been passed per rectum. There was a history of similar, less severe attacks every week for three months prior to admission. Because of anemia, iron had been given for a year, and during this time the stools had been black. The family history was noncontributory except for the mother's intussusceptions.

Physical examination on admission revealed that the child was acutely ill and lying on his right side with the legs flexed on the abdomen. The temperature was 101 F. and the pulse rate 140. The heart and lungs presented nothing remarkable. The abdomen was generally tender. There was a firm mass measuring 2 by 4 inches (5 by 10 cm.) in the midline just above the umbilicus. The mass was very tender, and peristalsis was absent. The red blood cell count was 1,660,000, with a hemoglobin content of 29 per cent. The white blood cell count was normal, as were the results of urinalysis. The preoperative diagnosis was intussusception.

*Operation.*—A paramedian incision was made on the right side. The small bowel was moderately distended. About 300 cc. of straw-colored fluid was encountered in the peritoneal cavity. A mass consisting of 15 inches (38 cm.) of invaginated small intestine was found, and it was thought that this was in the midjejunum. Reduction of the intussusception was attempted and found to be impossible. Resection of the area and end to end anastomosis were performed. The wound was closed in layers. During the procedure the patient received 300 cc. of blood.

After operation the child was extremely ill and was given another transfusion on the day after operation. Supportive treatment consisted of Wangenstein suction, use of penicillin and parenteral administration of fluids. The patient was able to take soft foods by the third postoperative day. Slight atelectasis developed and this was combated with flat hand percussion of the chest and with glucosulfamerazine® (sulfamerazine, 2 Gm., and sodium lactate, 2.24 Gm. per fluidounce [30 cc.] of glucose solution). The wound healed by first intention, and at the time of the patient's discharge the red blood cell count had risen to 4,660,000 and the hemoglobin reading to 85 per cent.

*Pathologic Report.*—The resected segment of bowel measured 98 cm. in length, 45 per cent of which was dark brown. An adenoma measuring 27 by 18 mm. was located at the head of the intussusceptum and showed intense congestion and degeneration. There was no evidence of malignancy.

*Progress.*—Recovery has been complete, and the patient now plays normally and no longer seems to be pale and run down.

## COMMENT

The rarity of an instance such as this is attested by the infrequency of reports concerning it. A survey of the literature revealed only 4 other records of intussusception due to familial occurrence of tumors of the small intestine. In a remarkable family reported by Sharber,<sup>20</sup> Roan,<sup>21</sup> Haggard and Floyd<sup>22</sup> and Miller,<sup>23</sup> 3 members underwent multiple operations for intussusception due to adenomas of the small intestine. All told, 9 resections were performed on 3 members of the family (father, son and daughter) for adenomas and intussusception. Van Dijk and Oudendal<sup>24</sup> reported a case of intussusception due to a neoplasm of the small bowel in which the patient's sister also had had a resection for intussusception. Gatersleben<sup>19</sup> described a case of multiple polyposis of the small intestine with repeated intussusceptions and cited 3 similar cases, in all of which a familial history had been obtained. Reisinger<sup>25</sup> cited 1 case in which three operations had been performed on 1 patient for recurring intussusception and in which the father had died seven years before of obstruction of the intestine by a mucous polyp. In addition, MacDermott<sup>26</sup> reported a case of resection of the ileum due to a polyp, in which case the patient's sister had a history of recurrent pain and passage of blood and mucus per rectum. In the cases recorded here, the first admission in case 1 was reported by Willis<sup>6</sup> in 1920.

It should be noted from these case reports that symptoms and signs directly attributable to the presence of the tumors in the small bowel had been present for a considerable length of time without recognition of their true nature. In both cases, multiple attacks of abdominal pain had occurred before the episodes which led to the emergency laparotomy. In both cases, unexplained anemia, with accompanying fatigue, had existed and almost certainly had been due to gastrointestinal hemorrhage, which had been unrecognized.

Dickson<sup>2</sup> emphasized "the obscure nature of the symptoms associated with tumors of the small bowel. These may suggest gallstone colic, renal colic, peptic ulcer, or *even a primary anemia*. Intussusception is a common complication. Celiotomy for intestinal obstruction reveals the true diagnosis often for the first time." Cassidy and Macchia<sup>18</sup> and

20. Sharber, A. L.: Report of a Case of Intussusception, J. A. M. A. **55**:907 (Sept. 10) 1910.

21. Roan, O.: Intussusception Due to Benign Tumors of the Small Intestine, Texas State J. Med. **27**:782, 1932.

22. Haggard, W. D., and Floyd, W. O.: Repeated Resections for Intussusception Due to Familial Tumors of the Small Intestine, Am. J. Surg. **28**:428, 1935.

23. Miller, C. M.: Adult Intussusception, J. Tennessee M. A. **32**:163, 1939.

24. Van Dijk, J. A., and Oudendal, A. J. F., cited by Oughterson and Cheever.<sup>9</sup>

25. Reisinger, cited by Haggard and Floyd.<sup>22</sup>

26. MacDermott, E. N.: Intussusception in the Adult Due to Tumors, Brit. M. J. **1**:1214, 1935.

Raiford<sup>27</sup> stressed the importance of roentgenograms, including the scout film and the gastrointestinal series, in establishing the presence of tumors of the small bowel. These authors, furthermore, emphasized the important differential point of achlorhydria in cases of tumor of the upper portion of the small bowel, in contradistinction to the hyperacidity of peptic ulcer.

In summarizing their paper on recurring intussusception caused by intestinal neoplasms, Oughterson and Cheever<sup>9</sup> listed the following admonitions:

1. Among the possible causes of irregular attacks of colic-like abdominal pain in adults, without obvious etiology, must be counted recurring intussusception.

2. In patients with such symptoms to remove a suspected but innocent appearing appendix, or to fix a harmlessly mobile kidney without careful examination of the intestinal tract, is poor surgery.

3. If an intussusception is found and reduced it is wise to assume that a tumor is present at the apex of the intussusceptum which should be removed.

4. If no tumor is found in connection with the intussusception, search should be made for one a short distance both proximally and distally.

5. If a tumor is found without intussusception, the intestine should be examined proximally and distally as another one may be present there.

6. In any case of intussusception due to tumor, the whole intestinal tract should be examined as thoroughly as possible, since tumors are often multiple and may cause recurrent attacks.

Every tumor of the intestinal tract, especially if the tumor is situated within the lumen of the intestine, no matter how benign the character of the growth, should be removed unless there is definite contraindication, since it always carries the threat of intussusception.

#### SUMMARY AND CONCLUSIONS

Intussusception, a relatively rare occurrence after the age of 2 years, is most frequently encountered in later life as a complication of tumors of the small bowel. Benign tumors are commoner than malignant growths in the small intestine; yet they are infrequently found, either clinically or pathologically. Adenoma is the most commonly encountered benign tumor of the small intestine. Intussusception occurs as a complication in about 30 per cent of cases of tumors of the small bowel.

Intussusception occurring in more than one member of a family as a result of adenoma of the small intestine is an unusual circumstance. Two case histories illustrating this interesting occurrence are presented. In both cases, symptoms directly attributable to tumors of the small bowel were exhibited but were not recognized as such prior to operation for intussusception. The association of recurrent attacks of abdominal pain with secondary anemia should suggest the possibility of tumor of the small bowel. Intussusception in the adult always is secondary to some underlying condition, usually benign tumor of the small intestine.

805 West Franklin Street (20).

27. Raiford, T. S.: Tumors of the Small Intestine, *Radiology* **16**:253, 1931.



## "EFFORT" THROMBOSIS OF THE AXILLARY AND SUBCLAVIAN VEINS

An Analysis of Sixteen Personal Cases and Fifty-Six Cases Collected from the Literature

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"EFFORT" thrombosis of the axillary, subclavian and, occasionally, brachial veins, although occurring infrequently, may be the consequence of either severe or unaccustomed exertion. This report is an analysis of 72 cases, 16 of which I have collected and 56 of which are assembled from a partial review of the literature<sup>1</sup> for the past ten years.

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(Footnote continued on next page)

"Effort" thrombosis was first reported in 1884 by von Schrötter.<sup>2</sup> By 1920, Cadenat<sup>3</sup> was able to collect 27 cases. Paggi,<sup>4</sup> in a review of the literature, found only 74 cases reported up to July 1933, and Matas<sup>1r</sup> in 1934 was able to cite 100 such cases. Veal, in 1940,<sup>5</sup> reviewing the literature for the last fifty years, was able to collect less than 150 cases and reported 17 of his own. His statistics are, however, subject to qualification, since he includes types of thrombosis other than "effort" thrombosis in his series. Only 4 cases could be so classified. In 1943 Veal and Hussey<sup>6</sup> reported 29 additional cases of thrombosis, but only 10 were of the traumatic or effort type. Undoubtedly many cases occur that are not reported. It is apparent that the occurrence of "effort" thrombosis of the upper extremity is infrequent clinically. In direct contrast, the incidence of intravenous clotting in the lower extremities is frequent. The literature also reflects the difference in thrombosis of the lower extremities and "effort" thrombosis as regards mortality. This difference hinges chiefly on the problem of pulmonary embolism in thrombosis of the lower extremities, which has been reported to occur in from 0.02 to almost 1.00 per cent of surgical cases.<sup>7</sup>

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Comments on Diagnosis, Pathogeny, and Treatment of this Lesion in Its Medico-Legal Relations, *Am. J. Surg.* **24**:642, 1934. (s) McClanahan, B. V.: Primary Thrombosis of the Axillary Vein, *ibid.* **30**:459, 1935. (t) Oldfield, M. C., and Pyrah, L. N.: Thrombosis of the Axillary Vein, *Brit. M. J.* **2**:68, 1936. (u) Perner, L., and Cohn, I.: Primary Thrombosis of the Axillary and Subclavian Veins, *Am. J. M. Sc.* **203**:340, 1942. (v) Sampson, J. J.: An Apparent Casual Mechanism of Primary Thrombosis of the Axillary and Subclavian Veins, *Am. Heart J.* **25**:313, 1943. (w) Stabins, S. J.: Primary Thrombosis of the Axillary Vein Due to Strain, *U.S. Nav. M. Bull.* **41**:1106, 1943. (x) Stover, L., and Herrell, W. E.: Extensive Thrombosis of the Right Subclavian and Axillary Veins Associated with Thrombophlebitis, Lymphedema, and Polycythemia Vera, *Proc. Staff Meet., Mayo Clin.* **15**:817, 1940. (y) Willicuts, M. D., and Shelburne, S. A.: Thrombosis of the Axillary Vein: Reports of Two Cases with Clinical Investigations, *U.S. Nav. M. Bull.* **41**:1730, 1943.

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3. Cadenat, F. M.: Thrombophlebitis of the Upper Extremities, *Presse méd.* **35**:253, 1920; cited by Eigen.<sup>1s</sup>

4. Paggi, B.: Thrombosi venose da sforzo degli arti superiori, *Policlinico (sez. chir.)* **40**:383, 1933; cited by Goldberg and Foley.<sup>1j</sup>

5. Veal, J. R.: Thrombosis of the Axillary and Subclavian Veins with a Note on the Post-Thrombotic Syndrome, *Am. J. M. Sc.* **200**:27, 1940.

6. Veal, J. R., and Hussey, H. H.: Thrombosis of the Subclavian and Axillary Veins: Report of Forty-Six Cases, *Am. Heart J.* **25**:355, 1943.

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In the upper extremity this complication practically never occurs.<sup>8</sup> It is on this basis that I am convinced that "effort" thrombosis is actually an inflammatory type of reaction in distinction to bland venous thrombosis. Its occurrence is frequently heralded by the marked and dramatic onset of acute vasospasm as exhibited by cyanosis, edema and pain. Its manifestations are more characteristic of a thrombophlebitis with fixation of the thrombus by an inflammatory reaction.<sup>1b</sup>

#### INCIDENCE

*Sex.*—The condition occurs principally in males. In the combined series of 72 cases there were only 12 females (16.7 per cent). These figures are weighted since my series was collected from groups consisting entirely of males. Consideration of the 56 cases collected from the literature showed 12 females, increasing the incidence to 21.4 per cent. Only a few cases involving females not included in this series have been reported in the literature.<sup>9</sup>

*Age.*—Although, in accordance with the definition of "effort" thrombosis, the greatest incidence is during the most active periods of life, with the highest peak in the 20 to 29 year age group, the condition can occur at almost any age. It has been reported at the age of 16<sup>1c</sup> as well as at the age of 66.<sup>1x</sup> It is significant that 56 patients were in the most active age groups (10 to 39), accounting for 77.8 per cent of the cases (fig. 1).

*Site of Involvement.*—Since "effort" thrombosis has been alluded to as a type requiring unusual activity or strain, one would expect the right subclavian and axillary veins to be most frequently involved, since most persons are right handed. In the 56 instances collected from the literature the condition was on the right in 37 (66.1 per cent) and on the left in 19 (33.9 per cent). In my series, it was on the right in 10 (62.5 per cent) and on the left in 6 (37.5 per cent) and in the combined

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8. (a) Moure, P.: Fracture de l'humerus, thrombose de la veine axillaire, embolie pulmonaire, Bull. et mém. Soc. anat. de Paris **89**:170, 1914; cited by Matas,<sup>1r</sup> (b) Moure, P., and Martin, R. H.: A'propos de la thrombo-phlébite par effort, Presse méd. **132**:371, 1932. (c) Schepelman, E.: Kasuistische Beiträge zur Venenthrombose mit besonderer Berücksichtigung, alterer und neuerer Theorien der Thrombose, Beihefte z. Med. Klin. **7**:23, 1911.

9. (a) Finkelstein, B.: Benigne Thrombose der oberen Extremität, Deutsche med. Wchnschr. **53**:198, 1927; cited by DeBakey, Oschner and Smith.<sup>1e</sup> (b) Firth, D., and Mackay, R.: Primary Thrombosis of the Axillary Vein with Recurrence, Lancet **2**:679, 1932. (c) Rosenthal, W. J.: Ueber Thrombose an der oberen Extremität nach Anstrengungen, Deutsche Ztschr. f. Chir. **117**:405, 1912; cited by DeBakey, Oschner and Smith,<sup>1e</sup> and by Sampson,<sup>1v</sup> (d) Veal, J. R. and McFetridge, E. M.: Primary Thrombosis of the Axillary Vein, Arch. Surg. **31**:271 (Aug.) 1935. (e) Winterstein, O.: Traumatic Arterial Spasm and Thrombosis of Subclavian Vein, Schweiz. med. Wchnschr. **55**:360, 1925. Cadenat.<sup>3</sup>

series on the right in 47 (65.3 per cent) and on the left in 25 (34.7 per cent) (fig. 2). Paggi<sup>4</sup> found that the ratio of involvement of the right and the left arm was 2.5 to 1, whereas in this combined series the ratio was less than 2 to 1.

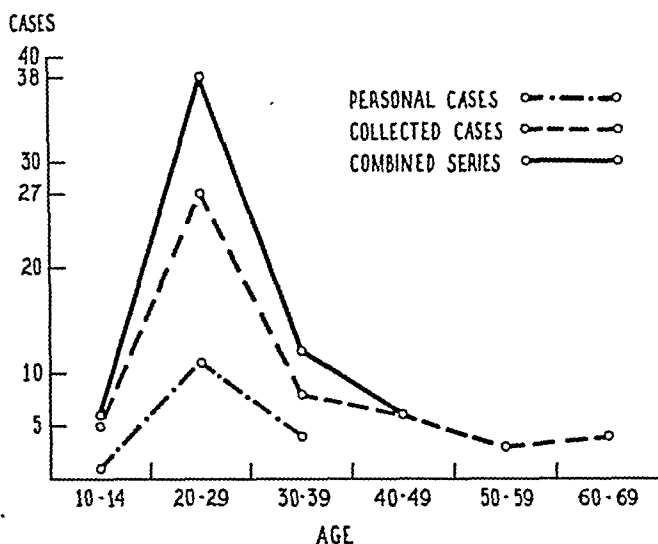


Fig. 1.—Age incidence.

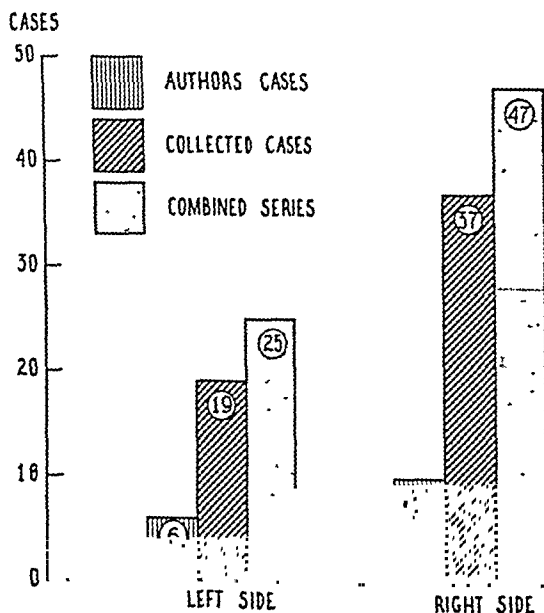


Fig. 2.—Side of involvement.

#### INCITING INCIDENT

Although the inciting or predisposing incident has been variously reported, it appears related to some unaccustomed strain or effort. However, there is a large group of cases in which no direct association,

such as pain, occurs between the effort and the thrombosis. This has been called idiopathic or spontaneous thrombosis, but it is probably related to effort, for most of the patients, when closely questioned, will relate some unaccustomed activity preceding the thrombosis. This occurred in 15 of the collected cases<sup>10</sup> and in 8 of my series, making a total of 23 among 72 (31.9 per cent). Additional reports of such occurrence have been made in the literature.<sup>11</sup> In the collected series throwing a baseball<sup>12</sup> was the next most frequently related action precipitating the thrombosis. This often incited a severe thrombosis of the effort type and occurred in 4 of the combined series (5.6 per cent of 72). A cause of additional magnitude was the lifting of heavy objects, which occurred in 4 of the collected cases<sup>13</sup> (7.1 per cent of 56) and in none of mine. The action varied from lifting a pail to lifting a heavy chunk of ice. This has also been reported in the literature elsewhere.<sup>14</sup> Heavy work preceded the thrombosis in 2 cases.<sup>15</sup> Infection of the upper respiratory tract was related to the thrombosis in 2 instances,<sup>16</sup> as was strenuous exercise in the gymnasium.<sup>16</sup> Other inciting factors occurring in 1 case each were as follows: pitching hay<sup>1b</sup>; pitching soybeans<sup>18</sup>; strenuously pulling on a wrench<sup>1w</sup>; breaking concrete with a sledge hammer<sup>1v</sup>; epilepsy attack<sup>1v</sup>; housework<sup>1v</sup>; sawing, planing and lifting wood<sup>1v</sup>; swimming<sup>1a</sup>; sawing a tree overhead<sup>1e</sup>; beating time with a baton<sup>1e</sup>; sawing wood<sup>1e</sup>; a fall on the hand<sup>1e</sup>; pushing a heavy object<sup>1p</sup>; basketball<sup>1p</sup>; direct trauma to the shoulder<sup>1u</sup>; sudden flexion of the elbow and backward pushing of the shoulder when a clutch slipped on the lever of a dredge<sup>1b</sup>; alcoholic bout<sup>1b</sup>; tennis<sup>1b</sup>; sudden forceful flexion of the arm when a wrench slipped<sup>1r</sup>; a fall of 30 feet (10 meters)<sup>1d</sup>; golf<sup>11</sup>; using an electrical cutting machine<sup>1v</sup>; working with a hammer<sup>11</sup>; putting in screws for curtain rods above the head<sup>11</sup>; placing jars on a shelf above the head<sup>11</sup>; cleaning a ceiling<sup>11</sup>, and a test of strength.<sup>1n</sup>

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10. DeBakey.<sup>1e</sup> Ditter and Walker.<sup>1f</sup> Eigen.<sup>1g</sup> French.<sup>1h</sup> Friedland and Farber.<sup>1i</sup> Goldberg and Foley.<sup>1j</sup> Gottesman and Beller.<sup>1k</sup> Gould and Patey.<sup>1l</sup> Kaplan.<sup>1o</sup> Oldfield and Pyrah.<sup>1t</sup> Pelnor and Cohn.<sup>1u</sup> Sampson.<sup>1v</sup> Kaplan.<sup>1p</sup>

11. (a) Pellot, J.: Les thromboses veineuses du membre supérieur droit, *Presse méd.* **11**:264, 1912; cited by Sampson.<sup>1v</sup> (b) Routier: Oedème subaigu du membre supérieur, *Bull. et mém. Soc. de chir. de Paris* **39**:1003, 1913; cited by Sampson.<sup>1v</sup> (c) Willan, R. J.: Three Cases of Axillary Vein Obstruction, *Edinburgh M. J.* **20**:105, 1918. Veal.<sup>5</sup>

12. Hoffert.<sup>1n</sup> Kaplan.<sup>1o</sup> Mason.<sup>1q</sup> Sampson.<sup>1v</sup>

13. Kaplan.<sup>1o</sup> Kaplan.<sup>1p</sup> Stover and Herrell.<sup>1x</sup>

14. Broca: Oedème subaigu du membre supérieur, *Bull. et mém. Soc. de chir. de Paris* **39**:1004, 1903; cited by Sampson.<sup>1v</sup> Winterstein.<sup>9e</sup>

15. Bruce.<sup>1e</sup> Gould and Patey.<sup>1l</sup>

16. Goldberg and Foley.<sup>1j</sup> Greenfield.<sup>1m</sup>

17. LeRiche, R: Traitement chirurgical des suites éloignées des phlébites et des grands edèmes non médicaux des membres inférieurs, *Bull. et mém. Soc. nat. de chir.* **53**:187, 1927; cited by DeBakey, Ochsner and Smith.<sup>1e</sup>

In my cases the causes were as follows: carrying a pack (2 cases) and (1 case each) climbing a rope, throwing rocks, pulling a propeller, a parachute jump, compression of the axilla with a figure-of-8 bandage for clavicular fracture and working with a wrench.

Additional etiologic agents reported in the literature are holding a high-spirited horse<sup>18</sup>; holding back a team of horses<sup>19</sup>; rowing a boat<sup>11c</sup>; struggling to hold an arrested person<sup>20</sup>; pulling up in bed<sup>21</sup>; loading and unloading a piece of field artillery<sup>22</sup>; long stirring of a heavy pudding mixture<sup>9b</sup>; scrubbing clothes for a long time<sup>5</sup>; carpentry work<sup>9e</sup>; throwing a ball or rock<sup>23</sup>; exercises of elevating arms overhead<sup>24</sup>; sleeping with the arms extended upward under the head<sup>6</sup>; moving heavy furniture<sup>25</sup>; pulling tents from trees,<sup>26</sup> and falling on the abducted arm.<sup>27</sup>

It would thus appear that although thrombosis of the axillary and subclavian veins can occur without apparent cause several conditions are conducive to its occurrence. These are principally some form of effort such as lifting, prolonged ordinary activity involving the arm or arms and shoulder girdle, strenuous physical activity involving these same structures, abduction of the arm such as in overhead activity, compression of the shoulder girdle and sudden violent backward motion of the shoulder girdle. The condition has also been described as occurring after disease such as pulmonary tuberculosis<sup>28</sup> and influenza.<sup>29</sup>

18. Schepelmann, E.: Demonstration eines Patienten mit Thrombose der linken Vena subclavia seltener Aetiologie, München. med. Wchnschr. **57**:2444, 1910; cited by Sampson.<sup>1v</sup>

19. Schwartz, E.: Oedème subaigu du membré supérieur, Bull. et mém. Soc. de chir. de Paris **39**:1002, 1913; cited by Sampson.<sup>1v</sup>

20. Delbet, P.: Oedème subaigu du membré supérieur droit, Progrès méd. **33**:186, 1918; cited by Sampson.<sup>1v</sup>

21. McGoogan, L. A., and Simmons, E. E.: Effort Thrombosis of Axillary Vein in Puerperium, Nebraska M. J. **18**:289, 1933.

22. Murad, J.: Phlébite par effort du membré supérieur, Bull. et mém. Soc. de chir. de Paris **39**:1001, 1913; cited by Sampson.<sup>1v</sup>

23. Finkelstein.<sup>9a</sup> Rosenthal.<sup>9c</sup>

24. Clute, H. M.: Idiopathic Thrombosis of the Axillary Vein, S. Clin. North America **11**:253, 1931.

25. Baum, H. L.: Die traumatische Venenthrombose an der oberen Extremität, Deutsche med. Wchnschr. **39**:997, 1913.

26. Schwindt, J. K.: Traumatic Thrombosis of the Upper Extremities, California & West. Med. **27**:635, 1927.

27. (a) Lahaussais, M.: Thrombophlébite traumatique aseptique, Presse méd. **18**:410, 1910. (b) Lowenstein, P. S.: Thrombosis of the Axillary Vein: An Anatomic Study, J. A. M. A. **82**:854 (March 15) 1924.

28. Blumer, G.: Report of Four Unusual Cases of Peripheral Venous Thrombosis, Yale M. J. **15**:296, 1908.

29. Jakobson, S.: Ueber einen Fall von Thrombose der Vena axillaris nach Influenza, München. med. Wchnschr. **78**:1017, 1931.

## PATHIOGENESIS

The interpretation of the pathogenesis is subject to a remarkable amount of confusion and will be reviewed only for the sake of completeness. This has been reported comprehensively by Eigen.<sup>18</sup>

Thrombosis may be precipitated by the following factors.

1. Phlebitis due to sudden stretching and compression of the vein.<sup>30</sup>
2. Rupture of the subclavius-axillary valve in the vein under the subclavius muscle (due to increase in venous pressure) by the sudden stretching of the subclavius muscle with the arm in abduction.<sup>11</sup>
3. Damage to endothelium caused by distention of the axillary veins resulting from respiratory effort.<sup>31</sup>
4. Injury to the intima as a result of pressure on the vein from the coracoid ligament and subclavius muscle with the arm extended and abducted.<sup>27b</sup>
5. Irritation of the perivenous sympathetic plexus, resulting in vasospasm and thrombus formation.<sup>32</sup>
6. Local venospasm resulting from stimulation of the sympathetic neurons, this being the end result of a reflex disorder.<sup>33</sup>
7. Chemical changes in the blood, caused by catabolites of abnormal metabolism in addition to whatever mechanical factors may be involved.<sup>34</sup>
8. Constriction of the subclavius vein below the head of the humerus and against the subscapularis muscle in hyperabduction of the arm.<sup>5</sup>
9. Stimulation of sympathetic nerve fibers resulting in a vasospasm of all corresponding blood vessels (both large and small). This stimulation is a reaction to a great many types of peripheral injuries.<sup>25</sup>
10. Thrombus formation resulting from compression of the subclavian vein produced by a posterior and cephalad rotation of the shoulder girdle without abduction of the arm.<sup>35</sup>

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30. Von Schrötter.<sup>2</sup> Willan.<sup>11c</sup>

31. Cadenat.<sup>3</sup> Lahaussais.<sup>27a</sup> Veal and McFetridge.<sup>9d</sup>

32. (a) Cottalorda, J.: La thrombo-phlébite par effort, *Lyon chir.* **29**:169, 1932; cited by DeBakey, Ochsner and Smith.<sup>1c</sup> (b) Hammann, W.: Zur Kenntnis der sogenannten Achselvenen Thrombose, *Zentralbl. f. Chir.* **67**:1871, 1940. (c) Löhr, W.: Ueber die sogenannte traumatische Thrombose der Vena axillaris und subclavia, *Deutsche Ztschr. f. Chir.* **214**:263, 1929; cited by De Bakey, Ochsner and Smith.<sup>1c</sup>

33. Homans, J.: Vasomotor and Other Reactions to Injuries and Venous Thrombosis, *Am. J. M. Sc.* **205**:313, 1943.

34. Löhr.<sup>32c</sup> Rosenthal.<sup>9c</sup>

35. Sampson, J. J.: Thrombosis of the Subclavian Vein, *Am. Heart J.* **19**:292, 1940. Sampson, J. J., and Capp, C. S.: Compression of the Subclavian Vein by the First Rib and Clavicle with Special Reference to the Prominence of Chest Veins as a Sign of Collateral Circulation, *Am. Heart J.* **25**:303, 1943. Sampson, J. J.; Saunders, J. B. de C. M., and Capp, C. S.: Compression of the Subclavian Vein by the First Rib and Clavicle, with Special Reference to the Prominence of Chest Veins as a Sign of Collateral Circulation, *ibid.* **19**:292, 1940. Sampson.<sup>1v</sup>

11. Hematoma in the axillary region compressing the axillary vein.<sup>36</sup>

12. Rupture of the intima or tears of small lateral vessels at the mouth of their collaterals by muscular action, based on the premise that the lesion is not situated primarily in the axillary or subclavian veins because their elasticity protects them from injury.<sup>11a</sup>

13. Theory of infection.<sup>37</sup> This is denied, since in some instances in which thrombectomy was done and the thrombus cultured organisms were not found.

14. Undue tightening (stretching) of the vein.<sup>38</sup>

#### DURATION OF TIME FROM PRECIPITATING EVENT TO MANIFESTATIONS

From a reviewing of the interval between the injury or precipitating event and the onset of symptoms and signs in 27 cases in which this

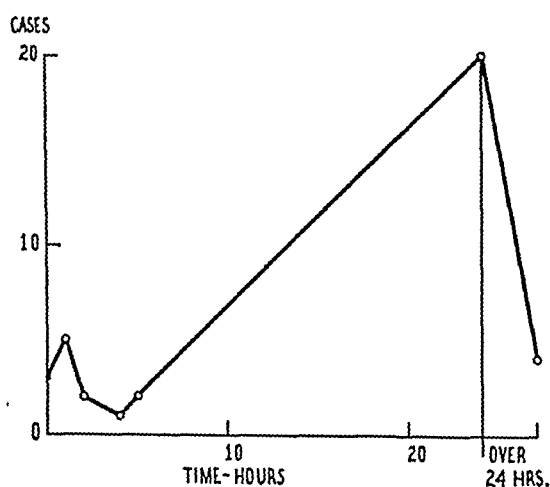


Fig. 3.—Duration of time from precipitating event to onset of manifestations.

was stated (fig. 3), it is evident that the majority occurred in the first twenty-four hours (23 cases, 85.2 per cent). In 10 (37 per cent) the onset was within one hour, and in 3 of these it was immediate. In only 4 did the onset occur after twenty-four hours.

36. Benda, cited by Löhr: Ueber die sogenannte traumatische Thrombose der Vena axillaris und der subclavia, *Deutsche Ztschr. f. Chir.* **214**:263, 1929. Moure and Martin.<sup>8b</sup>

37. (a) Chifolian, M., and Folliasson, A.: *Thrombo-phlébite à streptocoques due membré supérieur droit*, *Presse méd.* **40**:84, 1932; cited by DeBakey, Ochsner and Smith.<sup>1e</sup> (b) Grimaud and Dandelot: *Pathogénie de la thrombo-phlébite dite par effort*, *Presse méd.* **1**:108, 1924; cited by De Bakey, Ochsner and Smith.<sup>1e</sup> (c) Lecène, cited by Matas.<sup>1r</sup> Lenormant, C. and Mondor, H.: *Sur la prétendue; thrombo-phlébite par effort*, *Presse méd.* **2**:1669, 1931.

38. Triepel, H., cited by Benninghoff, A., in Möllendorff, W. V.: *Handbuch der mikroskopischen Anatomie des Menschen*, Berlin, Julius Springer, 1930, vol. 6, pp. 1 and 130, and by Franklin, K. J.: *A Monograph on Veins*, Springfield, Ill., Charles C Thomas, Publisher, 1937, p. 324.



## SYMPTOMS

The heralding symptoms were recorded in 51 of the collected cases and are noted in the author's 16 cases (table 1). Swelling was not only the most common heralding manifestation (35.8 per cent) but was also the most frequent on the patients' admission to the hospital, occurring in 61 cases (84.7 per cent). Pain initiated the occurrence of "effort" thrombosis in 32.8 per cent of cases and was likewise the second

TABLE 1.—*Heralding Manifestations (51 Collected Cases and 16 Personal Cases)*

Symptom	No.	%
Swelling.....	24	35.8
Pain.....	22	32.8
Cyanosis.....	4	6.0
Numbness.....	3	4.5
Prominent superficial veins.....	3	4.5
Aching.....	2	3.0
Discomfort in axilla and shoulder.....	2	3.0
Stiffness.....	1	1.5
Tightness.....	1	1.5
Tiredness.....	1	1.5
Soreness of arm muscles.....	1	1.5
Redness of extremity.....	1	1.5
Sensation of something giving in the arm.....	1	1.5
Coldness of the extremity.....	1	1.5

TABLE 2.—*Symptoms on Admission to the Hospital*

Symptom	No.	%
Swelling.....	61	84.7
Pain.....	36	50.0
Cyanosis.....	27	37.5
Prominent superficial veins.....	19	26.4
Numbness.....	12	16.7
Recurrences.....	10	13.9
Aching.....	9	12.5
Stiffness.....	8	11.1
Weakness of extremity.....	6	8.4
Tenderness in axilla.....	5	6.1
Paresthesia (tingling, burning).....	5	6.1
Heaviness.....	4	5.6
Tightness.....	4	5.6
Thrombosed cord in axilla.....	3	4.2
Easy fatigability of extremity.....	2	2.8
Redness of extremity.....	2	2.8
Soreness.....	2	2.8
Coldness.....	2	2.8
Fever.....	1	1.4
Tender vein.....	1	1.4

most frequent symptom on the patients' admission to the hospital (50 per cent). This parallelism is continued in the instance of cyanosis, which was the third most frequent heralding manifestation (6 per cent) and the third most common manifestation when the patients were first seen (37.5 per cent). Prominence of the superficial veins was the fourth most common initiating sign of thrombosis (4.5 per cent), as well as the fourth most common symptom (26.4 per cent). Numbness was of equal frequency (4.5 per cent) as an initial sign but was only fifth in frequency (16.7 per cent) of the manifestations when the patients were first seen. Discomfort in the axilla and shoulder and aching were of

equal prominence. Other heralding manifestations were stiffness, tiredness, tightness, soreness of the arm muscles, redness of the extremity, coldness of the extremity and the sensation of something giving in the arm.

#### EXAMINATION

A consideration of the physical examination in the combined series discloses that swelling was present in all the cases, with brawny edema present in 1 case<sup>1c</sup> (table 3). Other signs occurring in order of frequency are prominent superficial veins, cyanosis, palpable venous cord, coolness on the involved side, tenderness over the involved vein, fulness over the anterior part of the chest and shoulder and rubrocyanosis.

TABLE 3.—Symptoms Noted on Physical Examination

Symptom	No.	%
Swelling (brawny edema in 1 case).....	72	100
Prominent veins.....	54	76.4
Cyanosis.....	29	40.3
Palpable venous cord.....	23	31.1
Cooler on the involved side.....	9	12.5
Tender over axillary vein.....	8	11.1
Rubrocyanosis.....	6	8.4
Fulness over anterior region of the chest and shoulder girdle.....	6	8.4
Mottled skin.....	4	5.6
Lividity.....	4	5.6
Pitting edema.....	4	5.6
Fever.....	3	4.2
Rubor.....	3	4.2
Weakness of extremity.....	3	4.2
Warmer on involved side.....	2	2.8
Induration.....	2	2.8
"	2	2.8
"	2	2.8
"	1	1.4
Dry skin.....	1	1.4
Limited motion.....	1	1.4
Echymosis.....	1	1.4
"	1	1.4
"	1	1.4

#### SPECIAL EXAMINATION

Oscillometric determinations showed no notable variations, although 1 patient reported on in the literature stated that there was some diminution on the involved side.<sup>1d</sup>

Infra-red photographs merely confirmed the gross clinical findings.

Venous pressure was reported as greater on the involved side in 10 cases in which it was recorded. Venous pressure increasing with exercise, as reported by Veal and Hussey<sup>39</sup> in some cases, was recorded.<sup>1v</sup> This is substantiated by delayed emptying time of veins on elevation. This was confirmed in my cases.

Cutaneous absorption of sodium chloride was equal bilaterally in the case reported in the literature.<sup>1v</sup>

39. Veal, J. R., and Hussey, H. H.: The Use of Exercise Tests in Connection with Venous Pressure Measurements for the Detection of Venous Obstruction of the Upper and Lower Extremities, *Am. Heart J.* 20:308, 1940.

Blood sugar and carbon dioxide contents, determined in each extremity by Greenfield,<sup>1m</sup> proved to be equal bilaterally. Bronchoscopy was also performed in this case and revealed no abnormality. Oxygen saturation of the blood was first reported to be lower on the involved side by Horton.<sup>40</sup> This is also recorded by Pelter and Cohn<sup>1u</sup> and by Greenfield.<sup>1m</sup>

Other findings are recorded in a case of polycythemia vera by Stover and Herrel<sup>1x</sup> but are merely in keeping with this diagnosis.

In the present series determinations with the thermocouple done in the subsided stage showed the skin to be warmer on the involved side in 4 cases, although studies in the more acute stages reveal decreased temperature, indicating considerable vasospasm. This varies with the amount of superficial circulation. Sedimentation rates, clotting times and bleeding times proved to be uniformly normal.

A sterile blood culture is reported in 1 case.<sup>11</sup> The blood pressure was recorded in 6 of the collected cases<sup>41</sup>; in 3 the blood pressure was higher on the involved side, in 2 it was equal and in 1 it was lower. In the present series the incidence of increase and equality was approximately equal. This indicates that in a substantial number of cases there is an elevation of blood pressure on the involved side. Circulation time was recorded in 9 of the collected cases and has been determined in 9 of the present series. In every instance there was a delay of arm to tongue time on the involved side.

Phlebograms were reported in 19 of the collected cases and have been made in the present series as confirmatory of the clinical diagnosis of venous thrombosis. This is done by injecting 15 cc. of 35 per cent iodopyracet injection (diodrast<sup>®</sup>) into the antecubital vein and making a 14 by 17 inch (35.5 by 43 cm.) roentgenogram of the area under the arm and shoulder extending to the midline. A film should be exposed at this time and the injection continued, 15 cc. more being given and then another film exposed. A Buckey technic is the simplest method. In these circumstances the diagnosis is not difficult provided certain primary etiologic agents are excluded as primary causes.

#### DIAGNOSIS

The cardinal points in the diagnosis are as follows:

1. The history of unaccustomed or severe effort.
2. Initial manifestations of swelling and/or pain with cyanosis, prominence of superficial veins, numbness, coldness of the extremity, discomfort in the shoulder or aching.

40. Horton, B. T.: *Primary Thrombosis of the Axillary Vein*, J. A. M. A. 96:2194 (June 27) 1931.

41. Allin,<sup>1a</sup> Cohen,<sup>1d</sup> Ditter and Walker,<sup>1f</sup> Kaplan<sup>1p</sup> Matas,<sup>1r</sup> Sampson.<sup>1v</sup>

3. Swelling, prominence of superficial veins, cyanosis, palpable venous cord (may be tender), coolness on the involved side, tenderness over the vein or fulness over the anterior part of the chest.

4. Increased venous pressure.

5. Delayed circulation time.

6. Phlebographic evidence of venous obstruction.

In the differential diagnosis the following must be considered:

1. Thrombosis as part of a general disease: pyemia, septicemia, puerperal fever, typhoid, gout, polycythemia vera or heart disease.

2. Substernal goiter.

3. Mediastinal and intrathoracic tumors.

4. Aneurysms.

5. Cervical ribs.

6. Syringomyelia.

7. Central or peripheral neuropathic disorders.

8. Local external pressure.

It is obvious that these factors should be excluded as causes of thrombosis.

#### TREATMENT

The treatment (table 4) of this form of thrombosis was varied, with rest in bed and elevation of the extremity being the most commonly employed methods. Stellate sympathetic ganglion block was used in 14 cases to treat the vasospasm, which frequently develops as a severe primary manifestation with pain, coldness, cyanosis and even numbness. Another method employed to relieve vasospasm was heat applied to the extremity. DeBakey, Ochsner and Smith<sup>1e</sup> used sympathetic ganglion block in 4 cases with excellent results. Bruce<sup>1e</sup> favored this treatment. Barker,<sup>1b</sup> in reporting 6 cases, felt that during the acute stage simple treatment by rest, elevation of the arm and local hot moist packs is all that is indicated. This may be followed by the use of elastic compression bandages and graded exercises.

Foci of infection in dental and sinus locations were found in 3 of the present cases and removed. This is recommended by Oldfield and Pyrah.<sup>1t</sup>

Regional sympathetic ganglion block was utilized in the late cases, and although there was relief of the cyanosis and discomfort, there was no change in the edema. Other forms of treatment suggested have been multiple incisions,<sup>42</sup> needling to allow the edema to subside, throm-

42. Wilson, G.: Brachial Monoplegia Due to Thrombosis of Subclavian Vein, *Am. J. M. Sc.* **163**:899, 1922.

nectomy<sup>43</sup> and excision of the thrombotic segment.<sup>44</sup> The location of the thrombus may be in the subclavian, axillary, brachial and even jugular vein. By phlebography Pelter and Cohn<sup>1u</sup> showed the thrombosis to be in the subclavian vein at the inner border of the first rib in most cases. Veal<sup>5</sup> stated that in most instances the thrombosis involves the entire axillary vein, portions of the subclavian, basilic and brachial veins and occasionally the external jugular and the internal jugular vein. Roelsen<sup>45</sup> collected 24 cases (3 of his own) in which the axillary vein was explored, and 12 (50 per cent) showed no evidence of thrombosis. Operative removal of the thrombus has been recommended by some<sup>46</sup> to facilitate more rapid recovery, but this has not been borne out by the experience of others. Stabins<sup>1w</sup> favored its removal since, if allowed

TABLE 4.—Types of Treatment

Treatment	Literature	Present Series	Combined
Rest.....	19	7	26
Elevation.....	15	6	21
Stellate block.....	6	8	14
Hot packs.....	8 (6 moist)	4 (moist)	12
Compression (usually elastic).....	8	4	12
Ice packs.....	1	2	3
Physical therapy.....	1	1	2
Bronchoscopy.....	1	1	2
Massage.....	1	1	2
Sulfathiazole.....	2	0	2
Calcium lactate orally.....	2	0	2
Immobilization.....	2	0	2
Resection of axillary vein.....	1	0	1
Airplane splint.....	1	0	1
Alternate elevation and dependency	1	0	1
Infra-red irradiation.....	1	0	1
Exploration.....	1	0	1
Phlebotomy (case of polycythemia vera).....	1	0	1
Cast.....	1	0	1

43. Bazy, L.: Thrombose de la veine axillaire droite (thrombophlébite dite par effort): Phlébotomie; ablation des caillots; suture de la veine, *Bull. et mém. Soc. nat. de chir.* **52**:529, 1926. Biehl, M.: Thrombektomie bei blander Thrombose der Vena axillaris und subclavia, *Zentralbl. f. Chir.* **66**:1560, 1939. Lawen, A.: Ueber Thrombektomie bei Venenthrombose und Arteriospasmus, *Zentralbl. f. Chir.* **64**:961, 1937; cited by DeBakey, Ochsner and Smith.<sup>1e</sup> Schepelmann.<sup>18</sup>

44. Delbert, M.: Sur les thrombo-phlébites, *Presse méd.* **21**:549, 1913; cited by DeBakey, Ochsner and Smith.<sup>1e</sup> Huard, P. and Lenormant, C. H.: Un cas de thrombo-phlébite du membré supérieur révélée par un effort: Resection du segment veineux thrombosé et dénudation artérielle; guérison, *Presse méd.* **41**:1946, 1933; **42**:556, 1934; cited by DeBakey, Ochsner and Smith.<sup>1e</sup> Paggi, B.: Un raro caso di trombosi della vena ascellare destra (trombosi venose da sforzo), *Arch. ed. atti d. Soc. ital. di chir.* **39**:998, 1933; cited by DeBakey, Ochsner and Smith.<sup>1e</sup>

45. Roelsen, E.: So-Called Traumatic Thrombosis of the Axillary and Subclavian Veins, *Acta med. Scandinav.* **98**:589, 1939.

46. Grimault, L., and Dantlo, M.: Thrombophlébite dite par effort de la veine axillaire, *Bull. et mém. Soc. de chir. de Paris* **50**:118, 1924; cited by Sampson.<sup>1v</sup> Matas.<sup>1r</sup> Paggi.<sup>4</sup> Stabins.<sup>1w</sup>

to remain, the thrombus promotes future infection and "serious complications."

The end results of treatment are disappointing, although initial treatment of vasospasm may be dramatic. In 56 cases in which the results were stated only 13 patients had no residual effects (23.2 per cent). Residual swelling was a most prominent feature, with dilated superficial veins and considerable increase in swelling and discomfort on strenuous or unaccustomed activity. Several patients had to change their occupation. Recurrences are frequent, and in this series they were found in 10 cases (13.9 per cent). These may occur as late as after six years.<sup>25</sup> However, in many instances the swelling begins to subside after several weeks, the collateral venous circulation is soon established and the patient is fit to resume his old activities. Obviously the severity of the residual symptoms depends on the degree of preservation of collateral circulation.<sup>5</sup> In a series of 9 cases reported by Veal,<sup>5</sup> residual symptoms including weakness, early fatigue and pain in the arm after prolonged work or exercise occurred in 7. Sixteen patients observed by me all showed residual swelling, and only 2 were asymptomatic on activity.

Anticoagulants would seem to be of no value in the treatment of "effort" thrombosis, since the thrombosis establishes its full extent at once, and there is little tendency toward progression and practically none toward pulmonary embolism.

#### REPORT OF CASES

CASE 1 (axillary thrombosis).—S. L. was a physician, white, aged 37 years. In November 1942, while he was playing handball, pain and swelling of the right upper extremity suddenly developed, which subsided spontaneously within five days. In January 1944 he noted recurrence of the discomfort of the right upper extremity with swelling after a volleyball game. Roentgenograms taken at that time disclosed a benign bone cyst in the neck of the right humerus. The swelling and pain were aggravated by exercise, and he even noted tiredness of the extremity after writing for three to four minutes. He also observed tingling paresthesia with numbness. The condition gradually became worse. After discontinuance of the exercise, the pain and swelling subsided. It recurred each time he attempted active exercise. He was first seen by me on Feb. 18, 1945. By this time it was noted that the swelling was continuous, being greater on activity and dependency and in hot weather. The extremity was enlarged, the arm being  $1\frac{3}{4}$  inches (4.4 cm.) larger in circumference, the forearm  $\frac{1}{2}$  inch (1.27 cm.) larger and the wrist  $\frac{1}{4}$  inch (0.64 cm.) larger. There was notable dilatation of the superficial vessels. No arterial insufficiency was evident. The thrombosed vein was not palpable. The sedimentation rate was 12 mm. in 1 hour. Clotting time (Lee and White) was 9 minutes and bleeding time  $1\frac{1}{2}$  minutes. The venous pressure in the veins in the antecubital space was 28 cm. of water on the right and 17 cm. on the left. The arm to tongue circulation time, with injection of 3 cc. of 10 per cent calcium gluconate rapidly through a 19 gage needle, was 15 seconds on the right and 5 seconds on the left. Roentgenograms of the cervical region of the spine disclosed no cause for the thrombosis, and there was no cervical rib or evidence of scalenus anticus

syndrome. Phlebography (fig. 4A) confirmed the diagnosis of axillary thrombosis. Examination for foci of infection in the teeth, ear, nose and throat presented no positive findings. The cyst in the humerus proved to be small, and the orthopedic consultants felt that treatment was not indicated. Stellate ganglion block with procaine hydrochloride was performed three times, resulting in improvement of the edema of the extremity. However, the patient proved to be partially disabled.

CASE 2 (axillary thrombosis).—A. T., aged 36, Negro, noticed pain and swelling of the right forearm in October 1944, while cooking. In three weeks' time the swelling had increased to the point where he was unable to button his sleeves, and it had extended to the shoulder. He had been receiving anti-syphilitic therapy intravenously, and this may have been a factor. He also noted paresthesia, with weakness of the grip. On initial examination there was a 3 to 4 cm. enlargement of the extremity, with prominent engorgement of the superficial veins. Venous pressure was 38 cm. of water; blood pressures were equal, and circulation time was 20 seconds on the right and 12 seconds on the left with the use of calcium gluconate. A diagnosis of thrombosis of the



Fig. 4.—Thrombosis of the right axillary vein. A, case 1; B, case 2.

subclavian vein was made after phlebographic studies. Treatment at that time consisted of elevation of the arm, local application of heat and rest. This resulted in gradual improvement.

He was first seen by me in January 1945, when there was no apparent enlargement of the extremity, although there were some dilated veins present in the arm and several across the shoulder girdle. The sedimentation rate was 2 mm. in 1 hour. At this time he complained of some aching in the right shoulder. A phlebogram (fig. 4B) made with iodopyracet injection (diodrast<sup>®</sup>) showed axillary obstruction. There was no evidence of a focus of infection. By Jan. 25, 1945, the venous pressure was 29 cm. on the right and the circulation time, with 3 cc. of calcium gluconate injected rapidly, was 10 seconds on the right and 12 seconds on the left. This case is a good example of almost complete recovery from axillary thrombosis.

CASE 3 (bilateral thrombosis of the subclavian vein).—C. was a white man, aged 36 years, whose first thrombosis was of the right subclavian vein. In 1943, twenty-four hours after he received vaccinations for overseas duty in the army, redness, swelling and pain developed in the right arm and forearm. In the succeeding four days he noted progressing pain, swelling and heat involving the right forearm and wrist. He was treated with infra-red rays to the extremity and rest. Within one month he seemed to have recovered. This resulted in his separation from the service in the early part of 1944.

The second thrombosis, involving the left subclavian vein, occurred in 1947. Six days previous to his admission to the Veterans Hospital, Dallas, Texas, while on duty as a machinist's helper, he noted the sudden onset of numbness and tingling in his entire left upper extremity. The day before he had worked rather hard for a period of thirteen hours repairing a boiler. He noted progression of his symptoms as well as superficial venous distention, with some bluish discoloration of the extremity. Examination disclosed bilaterally distended superficial veins. These remained distended in a horizontal position on the left but collapsed on the right. The axillary vein was distended and tender. The left extremity was  $\frac{3}{4}$  inch (1.9 cm.) larger than the right. The blood pressure was 106 systolic and 60 diastolic on the right and 95 systolic and 54 diastolic on the left. The temperature of the skin was the same on the two sides. Venous pressure was 11 cm. on the right and 21 cm. on the left. Circulation time, with the use of 50 per cent magnesium sulfate, was 40 seconds on the right and 52 on the left. The extremity was elevated and stellate sympathetic ganglion block done, with improvement. Roentgenograms of the shoulder region and the chest, including an esophagram, were taken to rule

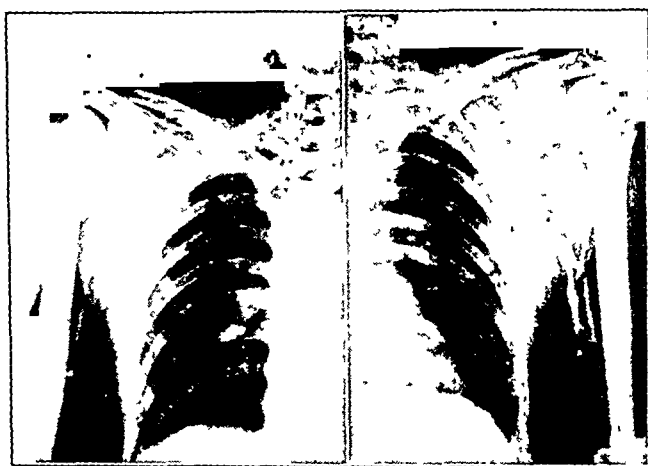


Fig. 5.—Bilateral thrombosis of the subclavian vein in case 3.

out other causes of venous thrombosis. A phlebogram (fig. 5) demonstrated bilateral thrombosis of the subclavian vein. The sedimentation rate, bleeding and clotting times and blood count were normal. The patient was instructed to refrain from severe manual labor and to use a compression bandage whenever the extremity became swollen.

#### COMMENT

"Effort" thrombosis of the axillary and subclavian veins occurs predominantly in males (83.3 per cent) in the active age group (77.8 per cent) and most commonly involves the right side (65.3 per cent). The inciting incident may merely be unaccustomed activity (31.9 per cent), pitching a baseball (5.6 per cent) or lifting heavy objects (5.6 per cent). It would appear that prolonged ordinary activity involving the arm or arms and the shoulder girdle, strenuous physical activity involving the same structures, abduction of the arm such as in overhead activity, compression of the shoulder girdle and sudden violent backward motion



of the shoulder girdle are additional factors. The pathogenesis of the condition has been outlined, and it is probable that several factors are acting simultaneously. Swelling (35.8 per cent) and pain (32.8 per cent) are the most frequent heralding manifestations. The swelling is usually gradual and unnoticed at first when a heralding manifestation, whereas the pain is sharp and severe as an initial symptom and is followed by swelling and cyanosis in from one-half to several hours. The swelling usually disappears by the tenth day, having become more severe by the third day. The introductory pain is usually in the shoulder and axilla and rarely along the course of the vein. In contradistinction to what occurs in thrombosis of the lower extremities, in which the distal portion of the extremity tends to swell initially, the most pronounced swelling is in the proximal portion, although the entire extremity may be involved. This swelling may be as much as 3 inches (7.6 cm.).<sup>14</sup> The initial symptoms must be due to spasm and obstruction. As soon as the spasm subsides and the collateral circulation becomes active, the edema will decrease (case 2 in Kaplan's series).<sup>15</sup>

The most prominent manifestations are edema, prominence of superficial veins, cyanosis, palpable venous cord, coolness of the involved side, tenderness over the involved vein, fulness over the anterior region of the chest and shoulder and rubrocyanois.

The blood pressure may be elevated on the involved side, the venous pressure increased, the circulation time retarded, the oxygen saturation of blood decreased and the temperature of the skin lowered.

Since the initial manifestations are secondary to vasospasm, treatment should be directed toward removing this element. Stellate sympathetic ganglion block with 10 cc. of 0.5 per cent procaine hydrochloride done by the anterior route seems to be the most direct attack on this factor. Elevation will control the edema in the early stages and compression in the later stages. Foci of infections should be eliminated and search made for primary causes of venous stasis and increased coagulability of the blood. In the present series the thrombus was most frequently in the subclavian vein rather than in the axillary vein. Despite energetic treatment, the late results have proved disappointing, with residual effects present in over 75 per cent of the reviewed cases. This emphasizes the need of early adequate treatment of this form of thrombosis with regional sympathetic ganglion block and elevation of the extremity followed by the use of compression bandages and gradual resumption of activity within the limitations of the recurrence of symptoms, particularly edema, which, if allowed to persist, will result in permanent incapacitation.

#### SUMMARY

A review of 16 personal cases of "effort" thrombosis of the axillary and subclavian veins and of 56 cases collected from the literature is presented.

## EFFECTS AND FATE OF BLOOD TRANSFUSIONS IN NORMAL DOGS

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IN MANY types of shock the use of blood transfusions is a time-honored method of attempting to correct the presumed disparity between the volume of circulating blood and the capacity of the vascular bed. Although considerable work has been done studying the effects of blood transfusions and other intravenously administered fluids in the treatment of shock, there is an incomplete understanding of what happens when a blood transfusion is given to a normal person or animal.

Boycott and Oakley<sup>1</sup> stated that after a transfusion of whole blood in dogs the plasma volume returns to normal in two to three days and the blood volume is increased for at least two days in proportion to the volume of red cells added. They also reported that the injected protein disappears from the blood stream within the same period. Krumbhaar and Chanutin<sup>2</sup> have reported similar results. According to Sibley and Lundy,<sup>3</sup> twenty-four hours after a blood transfusion in human beings the changes which occur in the blood represent only the effect of the addition of the red cells. Numerous workers have studied the effects of plasma transfusions in both normal patients and animals.

Since a blood transfusion is often given in anticipation of a shocking operation or as an emergency measure in the treatment of "shock" and since relatively little information is available in the literature concerning the immediate effects of transfusions in normal persons, it is felt that the present study may serve as a basis of a clearer understanding of the results which may be expected from blood transfusions during the time of administration and immediately thereafter.

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From the Department of Surgery, University of Utah Medical School.

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1. Boycott, A. E., and Oakley, C. L.: The Adjustment of Blood Volume after Transfusion, *J. Path. & Bact.* **38**:91, 1934.

2. Krumbhaar, E. B., and Chanutin, A.: Studies in Experimental Plethora in Dogs and Rabbits, *J. Exper. Med.* **35**:847, 1935.

3. Sibley, H. L., and Lundy, L. S.: The Blood Volume and Hemoglobin after Transfusion, *Surg., Gynec. & Obst.* **67**:490, 1938.

## METHOD AND CALCULATIONS

Donor blood, obtained under sterile conditions from normal healthy dogs, was citrated by adding 10 cc. of 2.5 per cent sodium citrate in isotonic sodium chloride solution to each 90 cc. of blood. In all the experiments here reported, transfusions consisted of freshly drawn, matched blood.

Recipient dogs were anesthetized lightly with 5 per cent pentobarbital sodium solution intravenously and prepared for the experiment by intubating the trachea, cannulating the carotid artery, exposing the femoral vein and catheterizing the bladder. Operative procedures were performed aseptically.

The following methods and calculations were employed:

*Hemoglobin Content.*—The photoelectric method as described by Evelyn and Mallory<sup>4</sup> was used.

*Hematocrit Value.*—This was measured in Wintrobe tubes centrifuged for 15 minutes at 3,000 revolutions per minute.

*Protein Concentration.*—The falling drop method of Barbour and Hamilton<sup>5</sup> was used. The specific apparatus and technic were checked against the micro-Kjeldahl and Biruet methods using a standard albumin solution.

*Plasma Volume and Blood Volume.*—These were determined by the dye method (T-1824)—Price and Longmire's modification of the Gibson and Evelyn technic.<sup>6</sup>

*Total Hemoglobin Mass, Circulating Cell Volume, Red Cell Size and Total Protein Mass.*—These were calculated as described by Price and his associates<sup>7</sup> and Metcalf.<sup>8</sup>

*Blood Pressure.*—A mercury manometer was attached to the carotid cannula and the mean arterial pressure recorded continuously on a kymograph.

*Nonprotein Nitrogen.*—The usual method of Folin and Wu adapted to the photoelectric colorimeter<sup>9</sup> was used.

*Respiratory Rate, Respiratory Volume and Oxygen Uptake.*—These were recorded and measured by means of a Sanborn "metabolism tester."

*Cardiac Output.*—This was determined by the direct application of the Fick principle.

*Arterial and Venous Oxygen Content.*—These were determined by Peter's and Van Slyke's method using a manometer Van Slyke apparatus.<sup>10</sup>

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4. Evelyn, K. A., and Mallory, H. T.: Micro-Method for the Determination of Oxyhemoglobin, Methemoglobin and Sulfhemoglobin, in a Single Sample of Blood, *J. Biol. Chem.* **126**:655, 1938.

5. Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method for Determining Specific Gravity, *J. Biol. Chem.* **69**:625, 1946.

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7. Price, P. B.; Hanlon, C. R.; Longmire, W. P., and Metcalf, W.: Experimental Shock: I. Effects of Acute Hemorrhage in Healthy Dogs, *Bull. Johns Hopkins Hosp.* **69**:327, 1941.

8. Metcalf, W.: The Fate and Effects of Transfused Serum or Plasma in Normal Dogs, *J. Clin. Invest.* **23**:403, 1944.

9. Notes on Operation of Evelyn Photoelectric Colorimeter, Philadelphia, Rubicon, 1939.

10. Peters, J. P., and Van Slyke, G. D.: Qualitative Clinical Chemistry, Baltimore, (Williams & Wilkins Company), 1932.

*Statistical Analysis.*—The experimental data were analyzed statistically by computing the standard error of all the means and testing the significance of the standard error of the difference between means when it was desired to show the significance of a curve.

## RESULTS

The following experiments were carried out on healthy anesthetized dogs to determine:

## A. Effects of anesthesia on controls.

1. No water given, 9 animals.
2. Water given by stomach tube, 3 animals. Isotonic sodium chloride solution given by vein, 1 animal.

TABLE 1.—Summary of Results of Control Experiments Showing Mean Values

	Hours					No. of Experiments
	0	2	4	6	8	
Hemoglobin (Gm./100 cc.).....	14.4 ± 0.3	15.2	16.0	16.2	16.7 ± 0.8*	9
Hematocrit value.....	42.3 ± 1.4	44.8	45.9	48.1	49.6 ± 1.7*	9
Protein concentration (Gm./100 cc.).....	7.25 ± 0.21	7.22	7.33	7.42	7.60 ± 0.22*	9
Plasma volume (cc./Kg.).....	50.3 ± 1.8	48.5	54.8	42.3	40.4 ± 1.4*	9
Blood volume (cc./Kg.).....	80.9 ± 2.9	84.0	78.2	75.2	73.6 ± 1.3*	9
Total circulating hemoglobin (Gm./Kg.).....	11.82 ± 0.59	12.50	12.50	12.30	12.45 ± 0.60	9
Total circulating protein (Gm./Kg.).....	3.58 ± 0.31	3.49	3.28	3.28	3.01 ± 0.09*	9
Circulating cell volume † (cc./Kg.).....	31.3	33.7	33.3	33.2	33.7 ± ...	9
Temperature.....	100.9 ± 0.4	98.5	100.5	100.5	102.5 ± 6.0	9
Pulse.....	189.0 ± 4.5	173.0	173.0	182.0	177.0 ± 4.8	9
Respiratory rate.....	15.3 ± 3.3	19.7	21.2	19.7	19.0 ± 2.0	9
Blood pressure.....	159.0 ± 4.0	149.0	153.0	156.0	148.0 ± 18.0	9
Weight (Kg.).....	20.0 ± 1.5	....	....	....	.....	9

\* Represents a significant difference between this mean and the initial mean.

† Circulating cell volume.

## B. Effects of transfusion.

1. No water given, 15 animals.
2. Water given by stomach tube, 3 animals.

## A. 1. Effects of Anesthesia Without Hydration on Controls.—

Nine dogs were anesthetized, and the previously described measurements were made over a period of eight hours. Table 1 summarizes the results. It will be seen that significant changes were observed in the hemoglobin, hematocrit level, plasma volume, blood volume, protein concentration, total hemoglobin mass, circulating cell volume and total circulating protein mass but that no significant changes were noted in the pulse, temperature, respiratory rate or blood pressure.

Figure 1 *A* represents graphically the changes in hematocrit level, blood volume and plasma volume in healthy anesthetized dogs over a period of eight hours. At the end of eight hours the increase in hematocrit value was 7.3 mm., or 15 per cent. The values obtained for hemoglobin concentration closely paralleled those for the hematocrit value. The plasma volume had decreased 19 per cent below its basal level by eight hours and the blood volume decreased 9.5 per cent. The reciprocal relationship of hematocrit value to plasma volume is well illustrated.

Figure 1 *B* represents changes in protein concentration, total circulating protein mass and total hemoglobin mass. Protein concentration

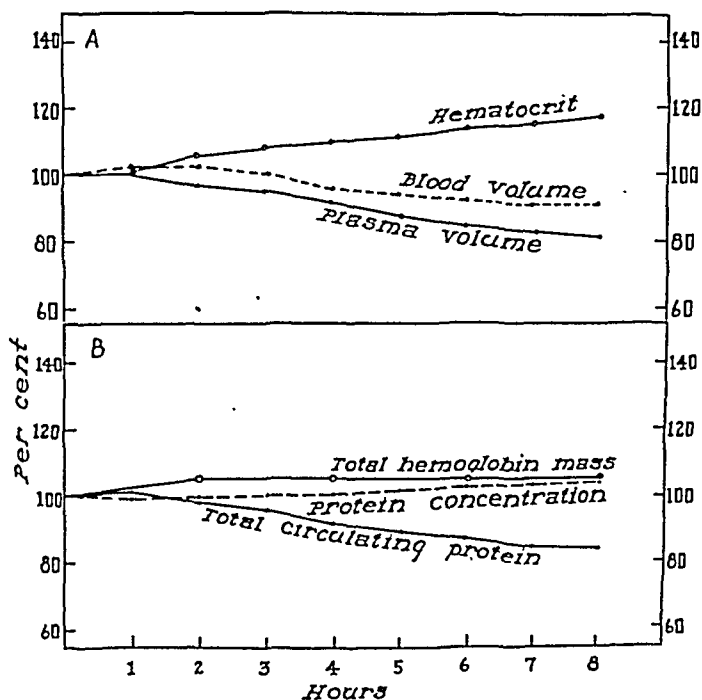


Fig. 1.—Control study. *A*, effects of eight hours of pentobarbital anesthesia and withholding water on hematocrit, blood volume and plasma volume of normal dogs. *B*, effects of eight hours of pentobarbital anesthesia and withholding water on total hemoglobin mass, protein concentration and total circulating protein mass of normal dogs.

gradually increased to 5 per cent above normal. The total circulating protein mass, however, decreased to 16 per cent below the original value, a disappearance rate of 2.9 per cent of the total per hour. By the end of two hours the total hemoglobin mass had increased 5 per cent. This increase was maintained until the end of the experiment. The circulating cell volume showed a curve similar to that of the total hemoglobin mass. There was no appreciable alteration in the mean size of individual red blood cells.

*A. 2. Effects of Anesthesia Plus Hydration on Controls.*—An entirely different set of values was obtained when the animals were kept hydrated during the eight hour period of anesthesia. The procedure just described was repeated in 3 dogs except that water was administered through a stomach tube at the rate of 3 cc. per kilogram per hour.

Although this series is small, it is evident that there was no pronounced tendency for plasma volume, blood volume or total circulating protein mass to decrease below the normal. Nor was there a significant increase of hematocrit value, hemoglobin or protein concentration.

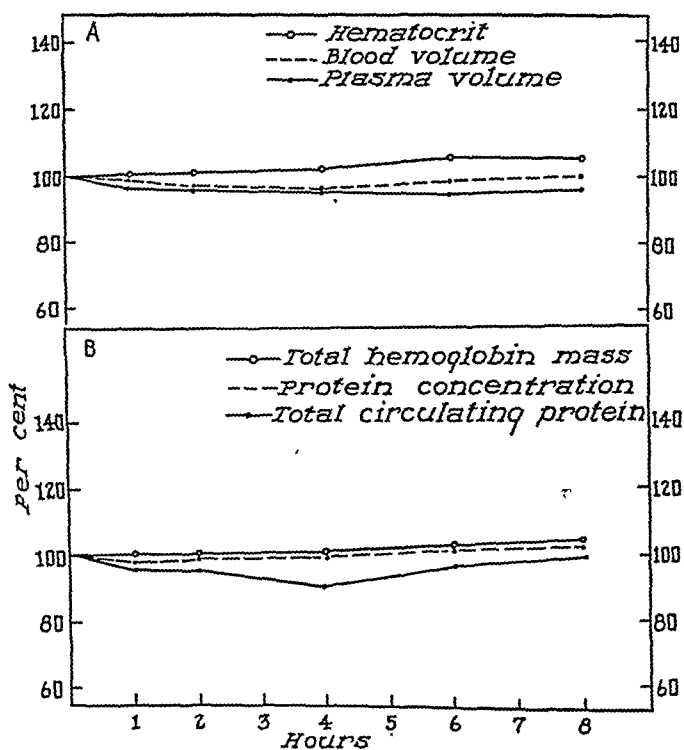


Fig. 2.—Control study. *A*, effects of eight hours of pentobarbital anesthesia and the administration of water through a stomach tube on the hematocrit, blood volume and plasma volume of a normal dog. *B*, effects of eight hours of pentobarbital anesthesia and the administration of water through a stomach tube on total hemoglobin mass, protein concentration and total circulating protein mass of a normal dog.

Figure 2 *A* shows the changes in hematocrit value, blood volume and plasma volume in a typical experiment. The increase in the hematocrit value was relatively slight and was probably due to increased total hemoglobin mass. Plasma volume and blood volume showed no significant alteration at the end of eight hours. During the experiment there were, however, minor fluctuations of the plasma volume amounting to as much as 5 per cent of the initial value.

Figure 2 *B* shows changes in protein concentration, total circulating protein mass and total hemoglobin mass. These values also remained relatively stable during the eight hour period.

In 1 experiment isotonic sodium chloride solution was given continuously by vein at the rate of 3 cc. per kilogram per hour. The results obtained were the same as when the water was given by stomach tube.

A comparison of figure 2 with the first figure demonstrates the effect of the administration of water. When water is given, all the measurements tend to remain relatively stable and the pronounced effects apparently due to dehydration do not occur.

*B. 1. Effects of a Blood Transfusion Without Supplementary Hydration.*—Fifteen dogs were used in this series, and the procedure employed was the same as for the controls except that a transfusion was given. Eight of the animals were intact, and 7 were splenectomized. The splenectomized animals were used in an attempt to eliminate the factor

TABLE 2.—*Values of the Citrated Blood Used for the 15 Transfusions*

Average hemoglobin .....	13.3 $\pm$ 0.7 Gm./100 cc.
Average hematocrit .....	38.0 $\pm$ 1.5 mm.
Average protein concentration.....	7.02 $\pm$ 0.17 Gm./100 cc.
Average amount of blood in each transfusion.....	275.0 $\pm$ 17.0 cc.
Average amount of plasma in each transfusion.....	158.0 $\pm$ 11.0 cc.
Average amount of plasma protein in each transfusion....	12.3 $\pm$ 0.7 grams
Average amount of hemoglobin in each transfusion.....	34.4 $\pm$ 2.8 grams

of the expansile canine spleen, which occasionally caused considerable change in blood volume during the first two hours of an experiment. No significant differences between splenectomized and nonsplenectomized animals were observed, however; so all have been included in the following summary.

Average values for the fifteen transfusions are given in table 2.

Table 3 gives in summarized form mean values obtained in this series of experiments. The basal period prior to the transfusion averaged two hours, and on the average sixty minutes was required to inject the blood. The third column of figures represents values obtained twenty minutes after cessation of the transfusion. In every case the effects of the transfusion were followed for five hours after its termination. For the sake of comparison, the values obtained from the series of control experiments are included in figures 6, 7 and 8. The period of the blood transfusion is indicated by a solid bar in the upper left hand section of each figure.

Figure 3 shows the changes in hematocrit value and protein concentration. As is evident, after transfusion both values increased at fairly

regular rates. In each case the value obtained at eight hours was equal to the percentage value of the control plus the percentage value of hemoglobin or protein added. Since the changes in the hemoglobin level paralleled those of the hematocrit reading, they are not shown.

Figure 4 represents changes in plasma volume and urinary output following transfusion. It will be seen that two hours after transfusion the plasma volume had returned to the pretransfusion level and five

TABLE 3.—*Summary of the Transfusion Experiments, Showing Mean Values*

	Hours							No. of Experiments
	0	2	3½	4	5	7	8	
Hemoglobin (Gm./100 cc.).....	15.9 ± 0.5	16.5	17.2	18.0	18.4	18.8	18.9 ± 0.4*	15
Hematocrit value (mm.).....	48.7 ± 1.5	50.1	53.8	55.5	56.5	57.7	58.0 ± 1.1*	15
Protein concentration (Gm./100 cc.).....	7.05 ± 0.12	6.96	7.18	7.28	7.54	7.57	7.57 ± 0.14*	15
Plasma volume (cc./Kg.).....	46.9 ± 1.2	47.0	53.9 ± 2.0*	51.6	46.6	41.5	40.1 ± 1.4*	15
Blood volume (Gm./Kg.).....	85.6 ± 1.9	88.0	106.0 ± 3.0*	101.0	97.5	89.0	83.9 ± 3.0	15
Total circulating hemoglobin (Gm./Kg.).....	18.4 ± 0.6	14.3	18.8 ± 0.7*	18.1	17.5	16.4	15.6 ± 0.6*	15
Total circulating protein (Gm./Kg.).....	3.30 ± 0.09	3.30	3.78 ± 0.15*	3.68	3.41	3.07	2.98 ± 0.03*	15
Circulating cell volume (cc./Kg.).....	37.6	39.8	52.0	52.9	49.9	46.5	45.5	15
Temperature.....	100.2 ± 0.3	100.8	101.0	101.3	101.8	102.3	102.0 ± 0.7*	15
Pulse.....	146.0 ± 7.0	152.0	152.0	150.0	146.0	153.0	158.0 ± 7.0*	15
Respiratory rate.....	11.5 ± 5.1	13.5	15.5	14.5	15.0	20.8	22.5 ± 5.1*	13
Respiratory volume (cc./Kg./min.).....	157.0 ± 25.0	198.0	194.0	190.0	205.0	236.0	258.0 ± 23.0*	10
Oxygen uptake (cc./Kg./min.).....	7.0 ± 0.6	7.6	7.7	7.8	8.2	8.6	8.6 ± 0.6	10
Blood pressure (mm. Hg.).....	145.0 ± 3.0	144.0	151.0	148.0	148.0	141.0	140.0 ± 4.0	10
Nonprotein nitrogen (mg./100 cc.).....	34.2	.....	.....	33.2	32.2	31.7	.....	3
Weight (Kg.).....	14.9 ± 1.2	.....	.....	.....	.....	.....	.....	15
Urinary output (cc./hr.)	12.8 ± 1.1	12.8	27.8*	50.5	20.4*	13.0	12.0 ± 1.3	10

\* Represents a significant difference between this mean and the initial mean.

hours after transfusion the plasma volume had decreased to 14 per cent below normal. This is a significant drop below normal; it is also a significant increase above what occurred in the control dogs at the same period. The urinary output was doubled during the hour of the transfusions and was increased fourfold for an hour after. The output returned to normal two hours after the transfusion.

The blood volume (fig. 5 A) returned to normal at the end of five hours; however, it was significantly increased above the blood volume obtained in the control series.



The total circulating hemoglobin mass showed an immediate increase of 40 per cent, which indicated a pronounced influx of red cells into the circulation over and above the injected donor cells. The total circulating hemoglobin mass then steadily decreased, until at the end of five

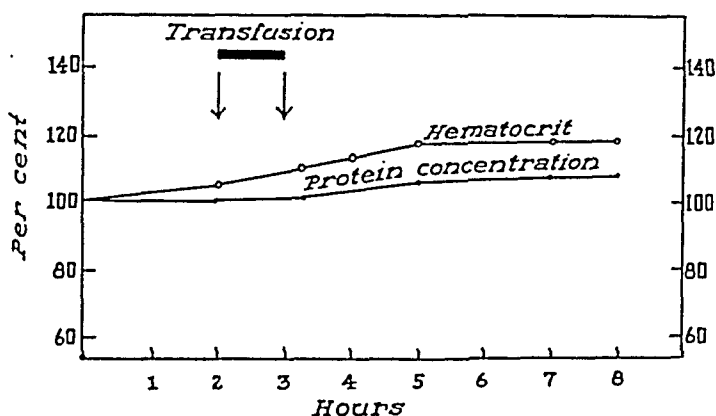


Fig. 3.—Effects of transfusions on hematocrit and protein concentration of healthy dogs anesthetized with pentobarbital. No water was given.

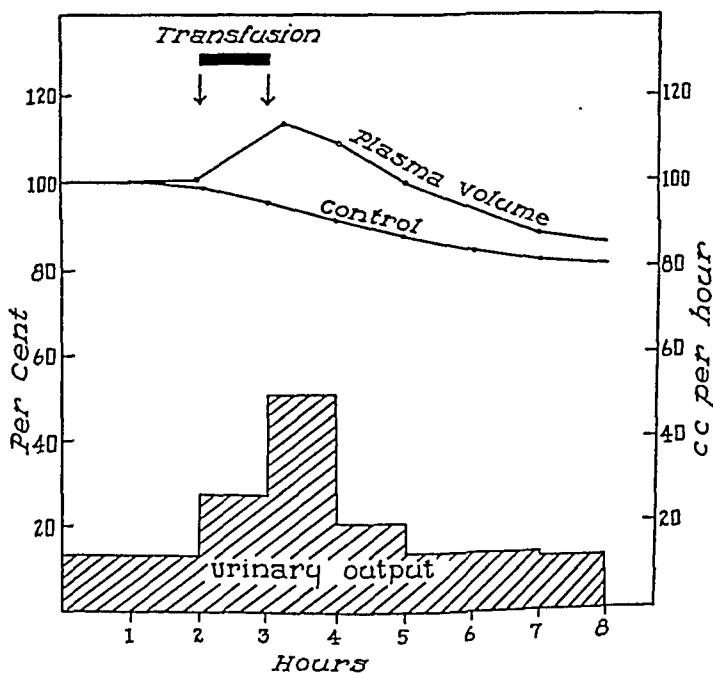


Fig. 4.—Effects of transfusions on plasma volume and urinary output of healthy dogs anesthetized with pentobarbital. No water was given.

hours the increase represented only the amount of injected red blood cells. The circulating cell volume showed a similar curve. No change was observable in the average size of red blood cells after the transfusion.

An interesting observation is that after the transfusion the total circulating protein mass gradually decreased. As shown in figure 5 *B*, after the initial increase following transfusion, the total circulating protein mass gradually diminished at such a rate that three hours after the transfusion an amount of protein equivalent to that injected had disappeared. At the end of five hours the total protein mass was 9 per cent below the pretransfusion level. This is a significant reduction; it is also a significant increase above what was obtained in the control experiments although the total amount of protein disappearing from the circulation after transfusion (1.32 Gm. per kilogram) was significantly

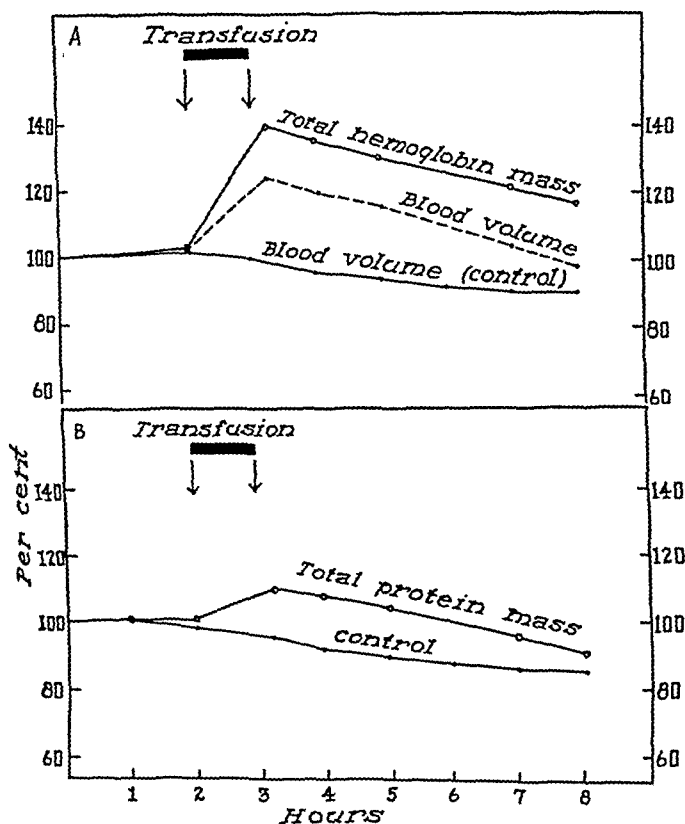


Fig. 5.—*A*, effects of transfusions on total hemoglobin mass and blood volume of healthy dogs anesthetized with pentobarbital. No water was given. *B*, effects of transfusions on total circulating protein mass of healthy dogs anesthetized with pentobarbital. No water was given.

greater than the amount (0.48 Gm. per kilogram) disappearing in the same length of time in the controls.

Significant increases were observed in temperature, respiratory rate and respiratory volume (fig. 6). It should be noted, however, that no effort was made to control the temperature of the dogs in the transfusion series, whereas in the series of control experiments which were performed in midsummer the dogs' temperature was controlled by

means of wet towels and an electric fan. Increase in oxygen consumption following transfusion was not significant. There was no significant change in blood pressure or pulse rate following the transfusion.

Plasma nonprotein nitrogen concentration was followed in 3 animals. No increase was noted after transfusion; on the contrary, an average fall of 8 per cent was observed four hours later.

No conclusive evidence could be obtained in 3 dogs indicating either increase or decrease in the cardiac output following transfusion.

*B. 2. Effect of a Blood Transfusion Plus Supplementary Hydration.*

—In an effort to reproduce the clinical problem in which many patients have an opportunity to drink water during the pretransfusion and post-transfusion period, 3 animals were given transfusions but, as in

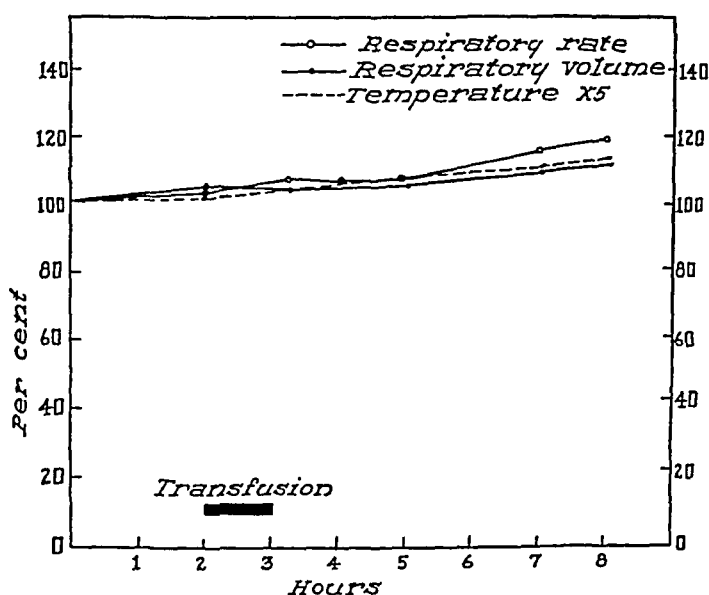


Fig. 6.—Effects of transfusion on respiratory rate, temperature and respiratory volume of healthy dogs anesthetized with pentobarbital. No water was given.

the case of the extra control dogs, they were given water through a stomach tube. Here again the results were different.

During the first two hours before transfusion, plasma volume and blood volume increased slightly. After transfusion the abrupt rise in plasma volume and blood volume was noted. This was followed by a rapid decline (fig. 7). The plasma volume returned to within 2 per cent of normal six hours after the transfusion but not below normal as was the case with the dogs which were not kept hydrated. The blood volume six hours after transfusion was still increased in excess of the mass of injected red cells. The hematocrit value (fig. 8) showed the usual increase immediately after transfusion, but then a leveling off was seen rather than a tendency to increase further. The urinary output increased

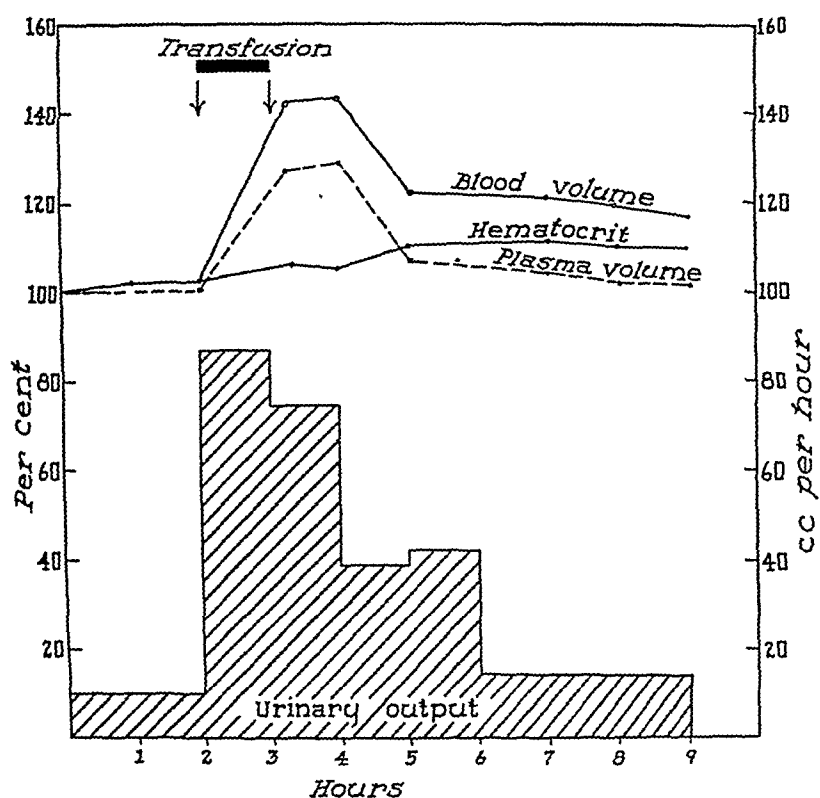


Fig. 7.—Effects of transfusion on blood volume, hematocrit, plasma volume and urinary output of a normal dog. Water was given through a stomach tube during the experiment.

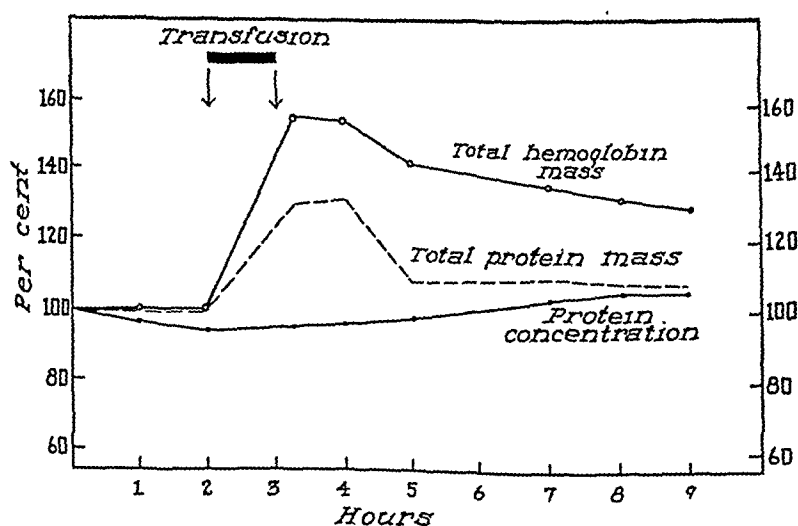


Fig. 8.—Effects of a transfusion on total hemoglobin mass, total protein mass and protein concentration of a healthy dog. Water was given through a stomach tube during the experiment.

eightfold during the transfusion and was increased sevenfold for the first hour thereafter. In the second and third hours after transfusion the output was four times normal, and then it returned to the normal range.

After the immediate increase following the transfusion the total protein mass (fig. 8) decreased rapidly and then leveled off at a value 8 per cent above normal. There was no tendency for the total mass of protein to fall below the pretransfusion level. The protein concentration showed a drop before transfusion and a gradual increase after the transfusion to 6 per cent above normal. The total hemoglobin mass increased rapidly to 55 per cent above normal, an increase of 40 per cent above that expected. It then decreased, until six hours after the transfusion it was 30 per cent above normal, an increase of 15 per cent above that expected.

There was no appreciable alteration of respiratory rate, temperature or blood pressure.

#### COMMENT

When normal healthy dogs are subjected to eight or nine hours of anesthesia, pronounced changes occur. Plasma volume, blood volume and total protein mass decrease below normal; the hematocrit value, hemoglobin, protein concentration and total hemoglobin mass increase (fig. 1). Except for the rise in total hemoglobin mass, these changes can be prevented by keeping the animal hydrated. Obviously the dehydration which occurs in animals during anesthesia is considerable and can produce significant changes in most of the values being studied here. The effects of transfusion in these experiments must be measured in relation to the base line of the effects of dehydration alone.

The most important change in the cellular elements of the blood following a transfusion occurred in the total circulating hemoglobin mass. Presumably the transfusion served as some type of impetus for erythrocyte depots to discharge their stores into the circulation, since immediately after the transfusion the total hemoglobin mass increased out of proportion to the amount of foreign red cells added. After this pronounced increase, the total hemoglobin mass gradually decreased to the expected value. As this occurred in splenectomized dogs as well as in nonsplenectomized dogs, it would appear that there is either a "reservoir" of red blood cells other than the spleen or the initial method of calculation failed to include cells which were made available after the transfusion. Although the spleen does serve as a sizable "reservoir" of red blood cells in the dog, evidence has been brought forward<sup>11</sup> which seems to show that "stores" of this nature do not occur in man.

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11. Ebert, R. V., and Stead, E. A · Demonstration That in Normal Man No Reserves of Blood Are Mobilized by Exercise, Epinephrine and Hemorrhage, *Am. J. M. Sc.* **201**:655, 1941.

It is to be expected that the fate of the injected cells is ultimately that of disintegration. Callender<sup>12</sup> has shown that in man the curve of destruction of transfused red blood cells is linear and that the average life is sixty days. This may be true of injected cells in dogs.

The plasma volume is not increased quantitatively for any length of time by the addition of the plasma in blood. As early as twenty minutes after the transfusion some of the fluid disappeared, and two hours later the plasma volume had returned to normal. Even in hydrated dogs (fig. 7) the plasma volume rapidly returned to normal. This initial translocation of fluid is rapid and is apparently an attempt on the part of the body mechanism to restore the plasma volume to a normal level. Since the excess urinary output accounted for one third of the lost fluid in the nonhydrated dogs and all the fluid lost in the hydrated dogs it is thought that this may be one of the main mechanisms for adjusting the plasma volume when it is increased by a transfusion.

Because of the influx of red cells into the blood stream the blood volume immediately after the transfusion was increased out of proportion to the amount of blood added. By the end of five hours, however, the blood volume decreased (because of decreasing plasma volume and total hemoglobin mass) until it was above the control only by the volume of the red blood cells added. This was demonstrated in the nonhydrated dogs. Why the total hemoglobin mass should remain increased above the expected value in hydrated dogs is difficult to explain.

The effect and fate of the injected protein is an intriguing problem. After transfusion the injected protein or its equivalent was rapidly removed from the blood stream. This occurred in the hydrated dogs as well as the nonhydrated dogs. In accord with Whipple's concept of a dynamic equilibrium between plasma protein and tissue protein, it is conceivable that this temporary excess of plasma protein is adjusted either by an increased rate of removal from the blood stream or by a decreased amount of plasma protein entering the blood stream, the rate of removal remaining constant. Although the fate of the injected protein is unknown, there are several possibilities: The protein may be catabolized; it may be partially broken down into large aggregates of amino acids and be resynthesized, or it may be stored as plasma protein. Howland and Harkins,<sup>13</sup> working with phlorhizinized dogs, have shown that injected plasma protein is not metabolized to amino acids before being utilized, as no excess nitrogen or sugar is found

12. Callender, S. T.; Powell, E. O., and Witts, L. J.: Life-Span of Red Cells in Man, *J. Path. & Bact.* **57**:129, 1945.

13. Howland, J. W., and Hawkins, W. B.: Protein Metabolism, Protein Interchange and Utilization in Phlorizinized Dogs, *J. Biol. Chem.* **123**:99, 1938.

in the urine. That conclusion is corroborated in the present series of experiments by the failure of the plasma nonprotein nitrogen concentration to increase after transfusion.

Since there is fairly good evidence for the existence of limited plasma protein stores<sup>14</sup> and most certainly for fairly large stores of plasma protein-building material,<sup>15</sup> it is possible that some of the excess protein enters those stores. Possibly the majority of the protein is broken down and resynthesized where needed. Some of the plasma protein may enter directly into plasma protein stores. Further work is being done in an attempt to ascertain the extent to which these stores can be built up by means of blood transfusion.<sup>16</sup>

#### SUMMARY

1. The immediate effects and fate of blood transfusions in normal dogs have been studied. The changes have been compared with those occurring in control animals during similar periods.

2. Pentobarital anesthesia for several hours produced significant changes in hematocrit value, hemoglobin, blood volume, plasma volume, protein concentration and total protein mass of normal dogs.

3. These changes were presumably due to dehydration, as they could be prevented by administration of water by stomach tube.

4. A blood transfusion given to nonhydrated dogs did not effectively increase the blood volume for more than five hours, the plasma volume for more than two hours or the total protein mass for more than three hours.

5. A blood transfusion given to hydrated dogs did not effectively increase the total protein mass or the plasma volume for more than two or three hours.

6. Immediately after a blood transfusion in nonhydrated dogs the blood volume was increased out of proportion to the amount of blood added because of an influx of red blood cells from depots into the circulation. After five hours, however, the net increase in blood volume was equivalent to the mass of injected red blood cells.

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14. Calvin, D. B.; Decherd, G., and Herrmann, G.: Plasma Protein Shifts During Diuresis, *Proc. Soc. Exper. Biol. & Med.* **44**:578, 1940. Beatie, J., and Collard, H. B.: Plasma Protein Storage, *Brit. M. J.* **2**:507, 1942.

15. Madden, S. C., and Whipple, G. H.: Plasma Proteins, Their Service, Production and Utilization, *Physiol. Rev.* **20**:194, 1940. Holman, R. L.; Mahoney, E. B., and Whipple, G. H.: Plasma Protein Regeneration Controlled by Diet., *J. Exper. Med.* **59**:251, 1934.

16. Seavers, R., and Price, P. B.: Effects of Sublethal Hemorrhage in Normal Dogs and in Dogs Previously Transfused with Whole Blood, *Surg., Gynec. & Obst.* **88**:178-184, 1949.

## SPONTANEOUS RUPTURE OF THE DISEASED SPLEEN

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**I**NTRA-ABDOMINAL hemorrhage, regardless of the cause, remains one of the most important of all the conditions constituting acute surgical emergencies. The ultimate result is the same whether the hemorrhage results from failure of diagnosis or from an error in judgment of the optimum time for operative intervention.

With the exclusion of bleeding of a genital organ in females and bleeding due to trauma, extremely difficult diagnostic problems remain. Included in these, all of which come under the category of "spontaneous intra-abdominal hemorrhage," are (1) rupture of an abdominal aneurysm; (2) rupture of a splanchnic vessel in patients with arteriosclerosis (abdominal apoplexy),<sup>1</sup> and (3) splenic rupture in either a normal or a diseased spleen. It is the latter of these with which this paper is primarily concerned.

Nontraumatic spontaneous rupture of an apparently normal spleen, although rare, is considered by some surgeons as a definite clinical entity. Dahle,<sup>2</sup> in reviewing the literature, found 14 cases and added 1 of his own. In the same year Lundell<sup>3</sup> reviewed 20 previously reported cases and came to the conclusion that a healthy spleen would not rupture spontaneously. Silverman and Randazzo<sup>4</sup> reported 1 proved case in 1946. McCoy<sup>5</sup> reported a case of spontaneous rupture which occurred during sleep.

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1. Cushman, G. F., and Kilgore, A. R.: Syndrome of Mesenteric or Subperitoneal Hemorrhage (Abdominal Apoplexy), *Ann. Surg.* **114**:672, 1941. Marks, M., and Freedlander, S. O.: Spontaneous Intra-Abdominal Hemorrhage, *ibid.* **121**:191, 1945.

2. Dahle, M.: Rupture of Normal Spleen Without Known Cause, *Acta chir. Scandinav.* **75**:519, 1934.

3. Lundell, G.: Spontaneous Rupture of the Spleen, *Acta chir. Scandinav.* **75**:547, 1934.

4. Silverman, I., and Randazzo, A. P.: Nontraumatic Spontaneous Rupture of the Spleen, *Arch. Surg.* **53**:355 (Sept.) 1946.

5. McCoy, J. C.: Splenectomy for Rupture of the Spleen: Report of Four Cases, *Ann. Surg.* **74**:13, 1911.



Spontaneous rupture of a diseased spleen is a definite pathologic entity. Noland and Watson<sup>6</sup> reported 3 cases of rupture occurring in a malarial spleen. Leighton<sup>7</sup> described a similar nontraumatic rupture of the spleen in a patient with malaria. Russ and Gaynor<sup>8</sup> reported a case of ruptured malarial spleen successfully treated by means of splenectomy in 1945. McCarthy and Knoepp<sup>9</sup> have reported 2 cases. In the first the rupture was caused by malaria, in the second it occurred in a patient with infectious mononucleosis and associated splenomegaly and in the third it took place in a patient with multiple hemangiomas involving the spleen. Darley, Black, Smith and Good<sup>10</sup> have reported a similar occurrence in a case of infectious mononucleosis. Thorpe,<sup>11</sup> in a personal communication, described a rupture which resulted from repeated attempts to palpate the spleen in a patient with infectious mononucleosis.

Conner and Downes<sup>12</sup> have reported a spontaneous rupture of the spleen in a case of typhoid. Splenectomy was performed, and the patient recovered. Similar splenic ruptures have been described as occurring in instances of acute leukemia,<sup>13</sup> sarcoidosis<sup>14</sup> and reticulum cell sarcoma with primary involvement of the spleen.<sup>15</sup>

Spontaneous rupture implies that there has been no history of trauma or that the degree of trauma has been so insignificant that it may not be considered as a causative factor. Of the many and varied diseases of the spleen which have led to ultimate spontaneous rupture, human malaria is undoubtedly the one of greatest import. This is especially true during the present period, with the growing reports of relapsing vivax malaria of Pacific origin occurring in veterans.

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6. Noland, L., and Watson, F. C.: Spontaneous Rupture of the Malarial Spleen: Report of Three Cases, *Ann. Surg.* **57**:72, 1913.

7. Leighton, W. E., cited by Conner and Downes.<sup>12</sup>

8. Russ, S. E., and Gaynor, J. S.: Spontaneous Rupture of a Malarial Spleen, *J. A. M. A.* **127**:758 (March 31) 1945.

9. McCarthy, A. M., and Knoepp, L. F.: Spontaneous Rupture of the Spleen, *Am. J. Surg.* **65**:413, 1944.

10. Darley, W.; Black, W. C.; Smith, C., and Good, F. A.: Spontaneous Splenic Rupture in Infectious Mononucleosis: Case and Pathologic Report, *Am. J. M. Sc.* **208**:381, 1944.

11. Thorpe, H. R.: Personal communication to the author.

12. Conner, L. A., and Downes, W. A.: Spontaneous Rupture of the Spleen in Typhoid Fever with Report of a Case Cured by Operation, *Am. J. M. Sc.* **147**:332, 1914.

13. Rubnitz, A. S.: Spontaneous Rupture of the Spleen Due to Acute Leucemia or Acute Leucemia Due to Trauma of Spleen . . . Which? Report of Case and Review of Literature, *J. Lab. & Clin. Med.* **28**:972, 1943.

14. James, I., and Wilson, A. J.: Spontaneous Rupture of the Spleen in Sarcoidosis, *Brit. J. Surg.* **33**:280, 1946.

15. Littlefield, J. B.: Spontaneous Rupture of the Spleen: Report of Three Cases, *Surg., Gynec. & Obst.* **82**:207, 1946.

Splenic rupture is as great a danger in patients with therapeutic malaria as in patients with acquired malaria. Bachmann<sup>16</sup> reported a case which occurred twenty-five days after the injection of 5 cc. of blood containing the plasmodia of tertian malaria, sudden death occurring during the second paroxysm. Twitchell<sup>17</sup> described a similar case in which rupture occurred after the patient had his eighteenth paroxysm of fever. The diagnosis was made by exploratory laparotomy; however, the spleen was not removed in view of the patient's poor condition. Postmortem examination confirmed the diagnosis.

It is generally conceded that there are two mechanisms which might be the cause of spontaneous rupture of a malarial spleen. The first, and least important, consists of a tear occurring in one of the fissures or through the parenchymal substance of the spleen without subcapsular hemorrhage. The second, and more frequent, consists of the formation of a subcapsular hematoma which ultimately ruptures. On consideration of the facts regarding the pathologic patterns followed by human malaria,<sup>18</sup> the events in either type become more apparent.

Malarial parasites, after entrance and dissemination throughout the body, tend to become localized predominantly in the organs possessing blood sinuses.<sup>19</sup> The most prominent of these is the spleen, which undergoes marked hypertrophy and hyperplasia. The splenic corpuscles show striking proliferative reactions. The lymphoid structures undergo toxic necrosis and grave depletion. Embolic occlusions of capillaries and arterioles result in punctate hemorrhages and toxic and necrotizing lesions throughout the spleen. The consequent boggy splenic pulp with its increased fragility in an already greatly enlarged spleen predisposes to spontaneous rupture of the first type. When a large vessel is involved, splenic infarction and/or hemorrhage may be sufficient to form a large subcapsular hematoma. The resultant disproportion between the size of the spleen and the resistance of the capsule predisposes to rupture of the second type.

The diagnosis should be suspected when the patient complains of spontaneous pain in the left side of the abdomen, followed by symptoms of peritoneal and/or diaphragmatic irritation coupled with

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16. Bachmann, F.: Spontaneous Rupture of the Spleen in Therapeutic Malaria, *München. med. Wchnschr.* **73**:528, 1926.

17. Twitchell, E. W.: Spontaneous Rupture of Spleen Following Malaria Therapy for General Paresis, *California & West. Med.* **33**:512, 1930.

18. Cannon, P. R.: Some Pathologic Aspects of Malaria, in a Symposium on Human Malaria, no. 15, American Association for the Advancement of Science, 1941.

19. Cannon, P. R.; Sullivan, F. L., and Neckermann, E. F.: Conditions Influencing the Disappearance of Living Bacteria from the Blood Stream, *J. Exper. Med.* **55**:121, 1932.

a clinical picture of hemorrhagic shock, and gives either a definite history of malaria, acquired or induced, with recent or recurrent relapses manifested by the usual paroxysm or a history of attacks of unexplained fever, accompanied with chills, headache and malaise following return from endemic areas. A definite diagnosis of malaria is difficult to make when the latter history is given. This is especially true in persons who have taken prophylactic antimalarial therapy during their stay in an endemic area and have discontinued it when they returned to their homes. For example, the patient in the accompanying case report had always assumed that his symptoms, which had manifested themselves after his return from the South Pacific, were due to malaria, but a definite diagnosis had never been made.

The physical findings parallel those in cases of ruptured spleen from any cause. These include signs of hemorrhage (low blood pressure, fast pulse, weakness, pallor, air hunger and restlessness); abdominal tenderness and rigidity, which may be generalized but is most pronounced in the left upper quadrant; rebound tenderness, with referral of pain to the left upper quadrant and/or the left shoulder; increased splenic dulness; a fluid wave, and Ballance's sign, or fixed dulness in the left flank due to the enlarging hematoma and shifting dulness in the right flank due to unclotted blood and serum.

Blood studies have proved of value. Demonstration of the malarial parasite in smears of the peripheral blood or of increasing hemorrhagic anemia, with a falling red blood cell count and hematocrit value, is most helpful. Leukocytosis may or may not be present.

The roentgenographic aids in the diagnosis of spontaneous rupture of the spleen are most important. Webb<sup>20</sup> reported an increased density in the left upper quadrant of the abdomen, elevation of the left side of the diaphragm, displacement of the stomach to the right and free fluid between loops of intestine. Zabinski and Harkins<sup>21</sup> described medial displacement of the colon. Solis-Cohen and Levine<sup>22</sup> and O'Neill and Rousseau<sup>23</sup> have described obliteration of the splenic shadow and a dilatation of the stomach with serrations of the greater

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20. Webb, in discussion on Foster, I. M., and Prey, D.: Rupture of Spleen: Analysis of Twenty Cases, *Am. J. Surg.* **47**:487, 1940.

21. Zabinski, E. J., and Harkins, H. N.: Delayed Splenic Rupture: A Clinical Syndrome Following Trauma, *Arch. Surg.* **46**:186, 1943.

22. Solis-Cohen, L., and Levine, S.: Roentgen Diagnosis of Lacerated Spleen, *Radiology* **39**:707, 1942. Levine, S., and Solis-Cohen, Survey Film Diagnosis of Rupture of Acute Surgical Abdomen, *Surg., Gynec. & Obst.* **78**:76, 1944.

23. O'Neill, J. F., and Rousseau, J. P.: Roentgenologic Examination of the Abdomen As an Aid in the Early Diagnosis of Splenic Injury, *Ann. Surg.* **121**:111, 1945.

curvature. These findings were present in the accompanying case reported and are well illustrated in the preoperative roentgenograms (fig. 1).

There is no question in regard to treatment. There is bleeding into the peritoneal cavity, and this hemorrhage must be controlled as quickly as possible. The only satisfactory method of accomplishing this is by splenectomy. The amount of blood lost in these cases may be staggering; therefore, adequate shock therapy is the most essential preoperative procedure. Whole blood is the replacement fluid of choice.<sup>24</sup> A muscle-splitting left rectus incision with a T-shaped extension into the left flank is preferred. The spleen is removed most easily by the technic first described by Balfour.<sup>25</sup> Dunphy<sup>26</sup> has recently published an excellent review of Balfour's basic contributions to this field.

#### REPORT OF A CASE

R. W., a 36 year old white soldier, a cook, was admitted to Fort Ord Regional-Station Hospital on Aug. 30, 1947. The chief complaint at the time of admission was severe pain in the left shoulder and left upper region of the abdomen of about seventeen hours' duration.

The patient had taken a nap the afternoon of the day before entry. Other than feeling extremely tired, which he attributed to recent long hours of work, he had no complaints. At approximately 4 o'clock he was awakened with a sudden excruciating pain in the left upper region of the abdomen and the left shoulder. During the interim, the pain persisted and became worse. The usual household remedies had been tried, with no results. The only relief was obtained by lying still in one position for long periods. Although he felt extremely tired, he could not sleep. Weakness of a notable degree gradually appeared. The abdominal pain spread to involve all four quadrants. A review of the systems revealed nothing remarkable. There had been no associated nausea or vomiting. The last bowel movement, the evening before admission, had been normal in character. The cardiorespiratory and genito-urinary systems were normal. No history of recent trauma of any kind could be elicited. The patient offered the history of unexplained fever accompanied with chills, headache and malaise of three weeks' duration. He also recalled intermittent sharp twinges of pain, of varying degrees of intensity, located in the left shoulder. The first of these had occurred two weeks prior to his entry to the hospital.

He reported to sick call at his dispensary at 8 a.m. on Aug. 30, 1947, where a diagnosis of spreading peritonitis secondary to a ruptured peptic ulcer was made. The hospital admitting officer obtained a surgical consultation with me immediately after the patient arrived at the receiving and disposition office.

The past history was not significant in any particular except for a story suggestive of recurrent attacks of relapsing malaria. During his service in New Guinea (1943) he had suffered several attacks of illness, primarily chills

24. Dunphy, J. E.: Shock: A Consideration of Its Nature and Treatment, *Brit. J. Surg.* **32**:66, 1944.

25. Balfour, D. C.: Splenectomy, *Surg., Gynec. & Obst.* **23**:1, 1916.

26. Dunphy, J. E.: Splenectomy for Trauma; Practical Points in Surgical Technic, *Am. J. Surg.* **71**:450, 1946.

and fever. He had not reported to sick call during any of these attacks. By comparing his symptoms with those manifested by other soldiers, he made a diagnosis of malaria and treated the disease by self medication (quinacrine hydrochloride [atabrine di-hydrochloride<sup>®</sup>], dosage not known). Since his return to the United States he had had several similar attacks, and each time he resorted to self treatment. No medication had been taken during the three weeks of illness just prior to his admission. There was no history of previous surgical intervention. The family history was not pertinent.

Physical examination showed the patient to be a spare white man, appearing much older than his actual age of 36 years. He was well developed but appeared to be in only a fair state of nutrition. There was evidence of recent loss of weight. He was extremely apprehensive and restless, tossing from side to side. The face was covered with beads of cold, clammy perspiration. A decided pallor was in evidence. There was no cyanosis. The temperature was 101.8 F. orally. The pulse rate was 100, and it was weak and thready. The respiratory rate varied between 26 and 30. At times a definite air hunger was evident. The examination showed an essentially normal condition except for the chest and abdomen. The left lower intercostal spaces were somewhat narrowed. There was a moderate lag of respiratory excursion of the left thoracic wall. The left side of the diaphragm was elevated on percussion. The pulmonary fields were clear throughout. The cardiac outline was not enlarged. Auscultation revealed a blowing systolic murmur, heard best at the apex. This was thought to be a murmur of the hemic type. The blood pressure was 90 systolic and 50 diastolic. The abdomen was markedly distended. Rigidity and abdominal tenderness were generalized but were most pronounced in the left upper quadrant and left flank. Rebound tenderness was present throughout, with referral of pain to the left upper quadrant and the left shoulder. Shifting dullness was demonstrated in the right flank. A large area of fixed dullness was found in the left flank. No fluid wave could be demonstrated. Auscultation revealed a completely silent abdomen. Rectal examination revealed generalized tenderness in the rectovesical pouch.

The pertinent laboratory findings were as follows: The red blood cell count was 2,200,000. The hemoglobin content was 50 per cent. The hematocrit value was 22. There was slight leukocytosis, with a moderate left shift. Malarial parasites (*Plasmodium vivax*) were demonstrated in smears of the peripheral blood. The urine was normal. An upright anteroposterior roentgenogram of the chest showed the left leaf of the diaphragm to be elevated (fig. 1). The right leaf was also slightly elevated. An upright scout roentgenogram of the abdomen (fig. 1) showed a large, oval, well circumscribed area of increased density in the left upper quadrant. The gastric air bubble was displaced medially. There were irregular serrations along the greater curvature of the stomach. The slightly distended large bowel was seen occupying a central position in the abdomen. It was surrounded by an area of increased density suggesting intra-abdominal fluid. Free fluid was also suggested by a similar density between the few loops of small bowel visualized and the homogeneous density extending from the extraperitoneal fat along the left gutter.

A diagnosis of intra-abdominal hemorrhage secondary to spontaneous rupture of a malarial spleen was made. Emergency splenectomy was advised.

During the interval before operation, a Levine tube was inserted. The patient received 1 unit of plasma and 1 pint (500 cc.) of whole blood prior to operation.

Laparotomy was accomplished two hours after his admission. After induction of anesthesia with thiopental sodium U. S. P. (pentothal sodium<sup>®</sup>), plus

curare for relaxation, a woven catheter endotracheal tube was inserted. Anesthesia was maintained by the use of a combination of pentothal sodium,<sup>®</sup> ether, nitrous oxide, oxygen and curare. The operating table was broken slightly at the level of the costal margin anteriorly and the body rotated slightly to the right and supported in this position by a sand bag in the loin. The abdomen was opened through a long paramedian incision splitting the left rectus muscle, with a T-shaped extension into the left flank. When the peritoneum was opened, a large amount of clotted blood was found in the left upper quadrant extending down into the left gutter. There was a large amount of unclotted blood and serum throughout the remainder of the abdomen. The liver was of normal size and appearance. The immediate field was cleared of blood and the spleen delivered into the wound by advancing the right hand along the free posterolateral aspect of the organ until the upper pole was reached; the spleen was then pushed into the wound. Diaphragmatic adhesions were minimal. The spleen was approximately five times



Fig. 1.—*A*, preoperative upright anteroposterior roentgenogram of the chest showing elevation of the left leaf of the diaphragm. *B*, preoperative upright scout roentgenogram of the abdomen showing a large, oval, well circumscribed area of increased density in the left upper quadrant. The gastric air bubble has been displaced medially. There are irregular serrations along the greater curvature of the stomach. The slightly dilated large bowel is seen occupying a central position in the abdomen and is surrounded by an area of increased density suggesting intra-abdominal fluid. A similar density may be seen between the few loops of slightly distended small bowel. Free intra-abdominal fluid is also suggested by the homogenous increased density extending from the extra-peritoneal fat along the left gutter.

the normal size. There were numerous subcapsular hematomas present over its posterolateral surface. There was a large subcapsular hematoma at the lower pole which occupied approximately one third of the diaphragmatic surface. There was a 3 cm. tear through the capsule at its uppermost extent near the anterior border. Fresh blood was oozing from this area. Splenectomy was accomplished without difficulty by means of Balfour's technic. The abdominal incision was closed with interrupted cotton sutures. One thousand cubic centimeters of whole blood was given during the operative procedure. The patient left the operating room in excellent condition, without evidence of respiratory embarrassment or circulatory failure.

In the immediate postoperative period a malarial paroxysm manifested itself in a severe chill followed by a rise in temperature to 106 F. Quinacrine hydrochloride therapy was instituted immediately, the parenteral route being utilized. A second malarial paroxysm occurred on the first postoperative day, at which time *P. vivax* was again demonstrated in smears of the peripheral blood. Repeated



Fig. 2.—Photograph of surgical specimen. The spleen measured 18 by 12 by 12 cm. At the operating table the capsule seemed under extreme tension. The organ was a deep bluish red and seemed to be less firm than the normal spleen in situ. Several subcapsular hematomas could be seen, the largest of which was located at the lower pole on the posterolateral surface. It measured 8 cm. in diameter and 2.5 cm. in thickness. *A* shows the splenic capsule turned back exposing the hematoma. The pointer demonstrates the approximate site of capsular rupture. The hilar surface *B* likewise showed several small subcapsular hematomas.

examinations since that time failed to show malarial parasites. Levine suction was continued for four days, during which time the patient was maintained on intravenous infusions of dextrose in isotonic sodium chloride solution, whole blood, plasma, amino acids and vitamins. A nonproductive cough, associated with signs of consolidation in the left lower pulmonary field, developed on the third

postoperative day. Stereoscopic roentgenograms of the chest led to the diagnosis of atelectasis of the lingular portion of the upper lobe in the left lung. This responded to conservative management, including frequent vigorous coughing, deep breathing exercises, administration of penicillin and ambulation. After discontinuance of gastric suction a modified liquid diet was tolerated. A soft diet was permitted on the fifth postoperative day and a full diet on the eighth day. The patient was made ambulatory on the third postoperative day. Healing of the wound was uncomplicated. He was discharged from the hospital on the fourteenth postoperative day without any complaints. At the time of his release the red blood cell count and the hemoglobin content were within normal limits

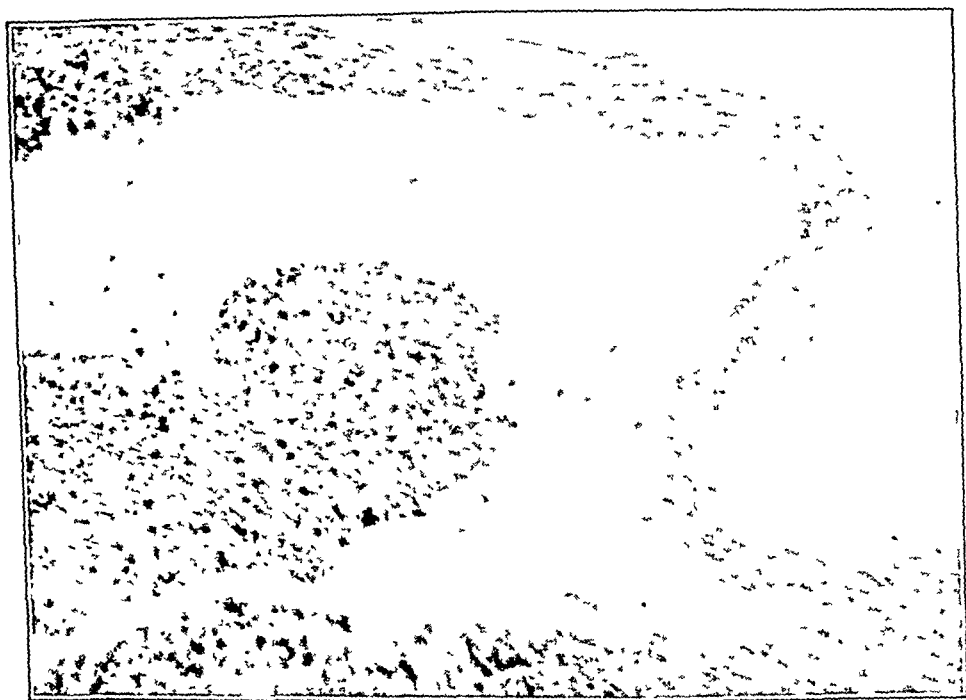


Fig 3—Photomicrograph of a section taken through the subcapsular hematoma near its periphery. Note how the developing hematoma has dissected the splenic capsule from the pulp.

Pathologic examination of representative sections through the spleen revealed a decided proliferative reaction of the splenic corpuscles (figs. 3 and 4). Evidence of toxic necrosis and depletion of the lymphoid tissue was noted. A great deal of malarial pigment was found deposited in the splenic pulp. Generalized fibrosis was present. Many parasitized erythrocytes were identified in small vessels and capillaries. Sections through the capsule revealed many small subcapsular hematomas. Figure 3 shows how the developing hemorrhage dissects the thickened splenic capsule from the pulp.

#### COMMENT

Beyond all doubt this represents a case of spontaneous rupture of a malarial spleen during a relapse of *P. vivax* malaria. There are several points illustrated which are of more than casual interest. Undoubtedly the subcapsular hematomas found at the time of opera-



tion had begun to form two weeks before the patient's admission to the hospital. I believe these to have been the explanation of the intermittent attacks of sharp pain in the left shoulder. Clinicians should be aware of splenic rupture, whether they are dealing with induced malaria or with acquired malaria, when clinical enlargement of the spleen is noted, accompanied with pain in the left shoulder. Rebound tenderness, with referral of the pain to the left shoulder, may be of value in making the diagnosis of splenic rupture, regardless of the cause.

#### SUMMARY

Evidence is cited from the literature and from a case reported to support the increasing incidence of spontaneous rupture of diseased spleens. It is suggested that there will be a further increase in the

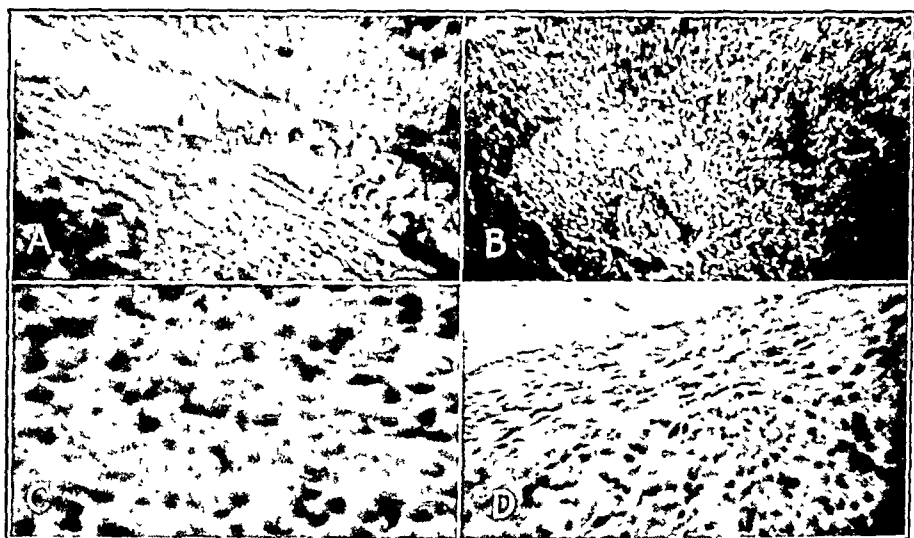


Fig. 4.—Photomicrographs of representative sections through the splenic pulp. Fixation in Zenker's solution (without acetic acid). Stained with hematoxylin-eosin azure II. *A*, many parasitized erythrocytes in a small vessel. *B*, proliferative reaction of a splenic corpuscle. Early toxic necrosis is in evidence. *C*, large amount of malarial pigment deposited through the pulp. *D*, generalized fibrosis and a greatly thickened capsule were found in all sections which were studied.

incidence of rupture of malarial spleens in view of the growing reports of relapsing vivax malaria of Pacific origin in veterans.

The pathologic changes in malarial spleens and the pathogenesis of their spontaneous rupture by two mechanisms are discussed in relation to previous reported cases and the pathologic findings in the accompanying case.

The outstanding clinical features are reviewed. Two clinical signs are emphasized. The first, intermittent attacks of pain in the left shoulder during a malarial relapse, should suggest the possibility of

the development of subcapsular hemorrhage. The second, rebound tenderness with referral of the pain to the left shoulder, is an aid in the diagnosis of splenic rupture, regardless of the cause.

The importance of competent roentgenologic assistance in the diagnosis is emphasized. Laboratory tests which may prove helpful in the evaluation of the patient's condition are listed.

It is pointed out that there is no question regarding treatment, splenectomy being the only method of controlling the hemorrhage. The preferred approach is given. Certain adjunct therapy, in particular that applicable to the treatment of hemorrhagic shock, is evaluated.

One case is presented in detail. Many of the technical factors involved in the preoperative preparation, anesthesia, the actual surgical procedure and the postoperative convalescence are presented. A gratifying recovery was noted, the patient being discharged from the hospital two weeks after operation with no symptoms.

# SYSTEMIC ADMINISTRATION OF HEPARIN AND DICUMAROL® FOR POSTOPERATIVE ADHESIONS

An Experimental Study

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**H**ERTZLER studied the peritoneum for many years and came to the conclusion that to prevent adhesions is to prevent healing. However, numerous investigators have utilized every imaginable modality, physical and chemical, to control the pathologic effects of adhesions. Many of the methods of procedure have been impractical and the results controversial.

In recent years, Ochsner and others experimented with digestive enzymes such as papain, claiming reduction in postoperative complications due to adhesions. Yardumia and Cooper advocated the use of pepsin intraperitoneally for the same purpose. Other digestants such as trypsin have also been tried.

The utilization of amniotic fluid concentrate (i. e., amfetin) as a stimulator of the peritoneal defense mechanism was investigated by Johnson, Warren, Lacy, Rea and Wangenstein, and favorable reports were published. Larson and Halverson introduced sodium ricinoleate as a peritoneal stimulant. Bargaen, Judd, Waldron and Steinberg proposed peritoneal immunization with killed vaccine suspensions of *Escherichia coli*. Seeley later studied the comparative stimulant effects of distilled water, amniotic fluid, Bargaen's vaccine and 2 per cent sodium ricinoleate by estimating the influx of polymorphonuclear cells into the peritoneal fluid and found that the figures were 19 per cent in six hours for distilled water and 36, 51 and 72 per cent respectively in three hours for the others.

Seeley stated that sodium ricinoleate caused an outpouring of exudate rich in *neutrophils and monocytes*, supplied fluid volume for lubrication and resulted in rapid phagocytic absorption of fibrin and regenerative

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Research project presented to the Department of Graduate Surgery of the New York Medical College, Flower and Fifth Avenue Hospitals, New York city, in application for a degree in surgery.

This project was approved by the Research Committee at its meeting of Jan. 26, 1945, for investigation. Part of this work was done in the Graduate Department of the college with the cooperation of Dr. J. H. Fobes, the director.

healing. Wangenstein reported on the use of 1 per cent ricinoleate in gastrointestinal anastomosis, with a 70 per cent preventative effect on the formation of postoperative adhesions.

Sweet was of the opinion that peritoneal stimulants and digestants are of questionable value.

Steinberg introduced coli-bactragen® (a tragacanth suspended vaccine) into the peritoneal cavities of 150 dogs, without adhesions forming. However, he stated that in some of the animals treated in the later stages of peritonitis, when damage to the tissue had already been incurred, adhesions did develop.

In 1941 Lehman and Boys reported on the use of heparin in the peritoneal cavity for the prevention of adhesions. Experimenting with dogs, they introduced 10,000 units of this drug in 300 cc. of isotonic sodium chloride solution followed by 5,000 units in the same amount of solution every twelve hours for a total of 40,000 units in three and a half days. They also reported on the intraperitoneal use of heparin in 14 human beings, with 1 death. They cautioned that the greatest potential hazard was hemorrhage.

Massie, reviewing the work of these authors, mentioned that experimental animals and controls were examined at the end of six weeks. When no drug was used, an incidence of adhesions of 130 per cent was found. In dogs in which isotonic sodium chloride solution, amniotic fluid and papain were utilized, an incidence of over 100 per cent was found. When heparin was employed, adhesions occurred in only 34 per cent. He advised the administration of 10,000 units every twelve hours for a total of 40,000 units in thirty-six hours. Seven cases involving human beings were reported in which good results were obtained. Massie cautioned that careful studies of the blood and clinical observations were required to guard against fatalities from hemorrhage and delayed healing of wounds.

Preliminary investigations in this project were directed along the following lines of thought:

A. An attempt was made to devise a practical method of keeping visceral and parietal peritoneal surfaces separated long enough for healing to occur. With pneumothorax and pneumoperitoneum in mind, it was thought that gas could be employed effectively, and in a similar manner postoperatively, to control the formation of adhesions. Furthermore, it seemed just as practical to give continuous intraperitoneal infusions of isotonic sodium chloride solutions and other fluids after operation as to give them intravenously. In addition, the mechanical and lubricating effects would be usable. The action of heparin infusions could also be studied.

B. An attempt was made to control the formation of fibrin by the systemic use of the newer anticoagulants, especially heparin and dicumarol.

The consideration that healing of wounds might be delayed in proportion to the limitation in the formation of adhesions was entertained. However, it was thought that early ambulation could be employed to affect the balance in favor of control of the adhesions, although sutures might have to be left in longer to prevent disruption of the wound.

At this point it might be well to review briefly the mechanics of the formation of intraperitoneal adhesions.

Histologically, the peritoneum is a three-layered membrane consisting of (1) a single cell layer of pavement epithelium, (2) a basement membrane of parallel connective tissue fibers plus cement substance and (3). an areolar connective tissue layer varying in density with the mobility of the viscera in different localities and carrying a network of blood and lymph vessels.

Anatomically, the chief concern is with the distribution of the parietal and visceral peritoneal linings, both normal and anomalous, and the mobility and configuration of the greater omentum. It should be remembered that these linings are everywhere contiguous.

Physiologically, two factors are particularly important in this connection. First, the peritoneum supplies mechanical lubrication to facilitate visceral mobility and function. Secondly, the absorptive capacity of the peritoneum is tremendous. Hertzler has shown that if a quantity of isotonic fluid up to 10 per cent of the body weight is instilled intraperitoneally, 30 per cent will be absorbed in one hour and up to 70 per cent in two hours. Use of hypotonic and hypertonic solutions did not alter these figures materially after osmotic equilibrium was reached. Accurate figures on the rates of absorption of gases were not obtainable although it is generally known that carbon dioxide, oxygen and nitrogen are more readily absorbed in the order given.

Pathologically, the origin of adhesions is always traumatic, whether they are due to chemical, physical, bacterial or toxic (malignant) injury. Immediately after injury to the endothelial cell layer there is an exudation of serum and fibrin. In two hours fibrin agglutination occurs. Firm bands are found in eighteen hours. Organization begins after the third day, with the transition of fibrin to connective tissue complete in six to eight days (Steinberg).

According to Hertzler, there are two types of adhesions, temporary and permanent. In the former there is no change in the basement membrane. Phagocytosis plus enzyme lysis causes spontaneous release in a few hours. This is a purely salutary process, nature's method of

limiting infection and inflammation. In some cases when these adhesions persist for longer than a few days they become much attenuated and may disappear later. In the case of permanent adhesions forming, however, there has been a permanent injury to the endothelium, with the formation of definite fibrin bridges which later become organized in firm connective tissue. Prenatal adhesions (so-called fetal peritonitis) are simple alterations in the development of serous surfaces and are usually of no pathologic consequence.

Surgically, the tendency of adhesions to form varies markedly in different animals and in the same animal under different conditions. The process appears to be related to the ability of the animal to form fibrin and lytic heparin-like substances in the intracellular fluids.

It is axiomatic that adhesions have no surgical significance unless they produce obstruction or other visceral disease.

The role of the greater omentum is important surgically and pathologically. It is practically always found adherent to previous peritoneal wounds, especially to incisions, and is frequently the cause of obstruction. It may be removed with impunity, and this has been suggested as a prophylactic measure. However, it has a definite useful function in the limitation of infection, encapsulation of foreign bodies and sealing of postoperative visceral wounds.

The second part of this project was concerned with the use of heparin and dicumarol systemically in retarding the formation of fibrin, with the hope that the incidence of adhesions would be reduced.

Heparin, a mucoitin polysulfuric acid in combination with acetic and glycuronic acids, is derived mainly from the mast cells of the liver and lungs. The first record of its anticoagulant properties was made by McLean. Howell purified it and worked on it until 1929. Best, of Toronto, later became interested in this substance and standardized its action quantitatively and physiologically. It is found normally in the circulating blood and is antagonized in the same medium by thrombokinase and trypsin. It is thought to have these main actions *in vivo*: 1. It inhibits platelet agglutination and prolongs coagulation time. 2. It prevents the conversion of prothrombin to thrombin. 3. It has a direct antithrombic action. The effect of heparin is manifested immediately on injection and persists for three or four hours. It does not affect fibrin already deposited, as in thrombus, nor does it affect osmotic pressures, red or white blood cells, hematocrit values, or antigens. Heparin is available commercially in solutions of 10 mg. per cubic centimeter (1,100 Toronto units), which quantity is sufficient to keep 5,000 cc. of plasma *in vitro* liquid for four hours at 37 C.

Heparin may be given intravenously, subcutaneously or intraperitoneally. For optimal effects the coagulation time should never fall

below 15 minutes or exceed 40 minutes (Lee-White method). Best and Murray have administered heparin by continuous intravenous injection (according to Prandoni) at the rate of 20 to 30 mg. per hour. Allen gave 50 mg. and repeated the same dose every four hours using an interrupted intravenous method. Evans and Boller are proponents of subcutaneous administration, using the Pitkin menstruum as a vehicle. The latter substance is composed of 18 per cent gelatin, 8 per cent dextrose and 1 to 1.5 per cent acetic acid in distilled water and serves to liberate the heparin much more slowly. Ampules containing 100 mg. of heparin per cubic centimeter of menstruum with or without vasoconstrictors added are obtainable. The average duration of effect with the former is forty-one hours and with vasoconstrictors (ephedrine and epinephrine) added sixty-one hours. Evans and Boller give 1 cc. of each for the first dose to a 150 pound (68 Kg.) patient. They also administer 200 mg. of dicumarol at the same time and then maintain the patient on about 100 mg. of dicumarol daily. Bauer has given 150 mg. of heparin every four hours intravenously and encountered no intra-abdominal, subcutaneous or other serious bleeding except for hematuria, which stopped in two or three days. Intraperitoneal administration has been described previously.

Dicumarol,  $C_{19}H_{12}O_6$  or 3,3'-methylene-bis-(4 hydroxycoumarin), was isolated and synthesized by Link in 1940. When given orally its action is to produce hypothermia. The disodium salt has been used intravenously for the same purpose. Dicumarol prolongs the prothrombin time, increases the sedimentation rate, impairs clot contractility and in large doses prolongs coagulation time. The anticoagulant activity of dicumarol is delayed until there is a considerable reduction in free blood prothrombin, which takes from twenty-four to forty-eight hours. The first dose is figured on the basis of 2 mg. per pound (average, 300 mg. in human beings). Successive doses must be based on the prolongation of the prothrombin time over the normal, which is from 10 to 15 seconds. The Quick method is used most frequently, and the result is best expressed in percentage of normal. Bleeding rarely occurs when the prothrombin time is 10 per cent or more, and thrombosis is retarded when it is over 30 per cent of normal. Dicumarol has a cumulative action which may carry over for many days, and its dosage is not related to age and weight. Its site of action is unknown, and it has no anticoagulant action *in vitro*.

The experimental investigations which are to be described were carried on over a period of about three years. A total of one hundred and eight procedures was performed on 37 mongrel dogs varying in weight from 18 to 42 pounds (8.2 to 19.1 Kg.). The youngest animal was about 3 months old and the oldest over 8 years.

The investigation was carried on in two parts. First, it was planned to study the mechanism of the formation and control of adhesions by repeating procedures already described in the literature. The second part was devoted to the attempt to limit the production of adhesions by administering heparin and dicumarol systemically.

The modern surgical principle of early ambulation was perforce utilized throughout. The only animals to which this did not apply were those kept partially anesthetized during prolonged intraperitoneal infusion procedures.

#### PART ONE

This was devoted to the study of (a) peritoneal closure and constricting dressings and (b) intraperitoneal instillation of gases and liquids. Thirteen dogs were subjected to a total of fifty-seven operative procedures.

*A. Peritoneal Closure and Constricting Dressings.*—The observations on method of peritoneal closure and type of dressing were considered as part of the instillation operations, except when gases and heparin were used intraperitoneally. Twenty-eight procedures considered in groups of seven were performed. Two methods of peritoneal closure were employed. In the first two groups the usual continuous approximation suture was used. The remaining peritoneal closures were effected by interrupted sutures placed about  $\frac{1}{2}$  inch (1.27 cm.) apart, with careful eversion of the peritoneal edges. In all cases the greater omentum was pulled down and interposed between the viscera and the incision. The effect of constricting abdominal dressings was observed simultaneously by utilizing them in groups 1 and 3.

A preliminary operation was performed on each dog for the purpose of producing adhesions. No special preoperative or postoperative supportive measures other than routine feeding and watering were used. Each animal was given a proportionate dose of morphine sulfate hypodermically to quiet it and then anesthetized with intravenously administered thiopental sodium (pentothal sodium®), occasionally supplemented with open cone ether. Epilation was performed chemically by a saturated solution of barium sulfide and the skin prepared with soap, ether, iodine and alcohol. Aseptic technic was followed as closely as possible. A mid-line celiotomy through a 4 or 5 inch (10 to 12 cm.) incision was then performed. Careful exploration was carried out and particular notice taken of congenital or other preexisting adhesions or bands. The presence of existing inflammatory processes, especially pyometra (canine salpingometritis) was also noted on the animal's record card. A loop of bowel was picked up and the serosa rubbed vigorously with dry gauze until it was red, and  $2\frac{1}{2}$  inch (6 cm.) marker sutures of white cotton were then placed at each end of the traumatized area and the



loop dropped back into the abdominal cavity. The wound was closed in three layers, chronic gut for the peritoneum, interrupted cotton sutures in the fascia and continuous subcuticular plain gut for the skin. Particular attention was paid to the method of peritoneal closure (to be described later). The wounds were then sealed by painting with rubber cement and applying crinoline in successive layers and either covered with a circular moderately constricting bandage or reenforced with short straps of flamed adhesive.

The results of these twenty-eight observations were as follows:

Group 1 (7 cases; continuous peritoneal closure and constricting bandage). In this group there were firm adhesions between the peritoneal scar and the greater omentum in every case. In 3 instances loops of bowel were found adherent in addition.

Group 2 (7 cases; continuous peritoneal closure and wound sealed with rubber cement and crinoline). Visceroparietal adhesions were seen in 4 instances. The adhesions appeared less firm and more elastic.

TABLE 1.—*Influence of Method of Peritoneal Suture and Type of Wound Dressing on the Incidence of Visceroparietal Adhesions*

Type of Suture and Dressing	Incidence of Visceroparietal Adhesions, %
Group 1 (continuous suture plus constricting dressing).....	100
Group 2 (continuous suture plus wound seal).....	57
Group 3 (interrupted, everting sutures plus constricting dressing).....	71
Group 4 (interrupted, everting sutures plus wound seal).....	28

Group 3 (7 cases; interrupted, everting peritoneal closure and constricting bandage). Visceroparietal adhesions were found in 5 cases, an improvement over group 1. The adhesions were short and firm as in group 1, however.

Group 4 (7 cases; interrupted peritoneal closure and wound seal). Adhesions between the omentum or the bowel and the peritoneal incision were seen in only 2 instances. They appeared longer and more elastic, similar to those in group 2.

Conclusions: 1. Careful eversion of the incised peritoneal edges in the closure of wounds tends to decrease the incidence of visceroparietal adhesions. The continuous over and over suture, particularly if placed under tension, leaves a visceral edge of raw peritoneum and suture material to which intra-abdominal structures are prone to adhere. 2. The common practice of applying constrictingly long straps of adhesive postoperatively should be discouraged. This tends to press together the raw parietal and visceral wounds and encourages the formation of dense short adhesions capable of producing a pathologic

process. 3. Best results were obtained in this group of procedures when the peritoneum was carefully everted and a simple wound-sealing dressing was applied.

No mention is made of the incidence of viscerovisceral adhesions at this time. They occurred practically 100 per cent of the time and are to be discussed further in detail.

*B. Intraperitoneal Instillation of Gases and Liquids.*—The original group of 13 dogs were subjected to forty-four procedures. The operative technic used was the same as before with the exception that suturing bites were placed close together to produce leak-proof closures. Incisions were made through the right or left rectus muscle parallel to the original scar. A record was made of all adhesions found; they were then carefully separated and peritonealized as much as possible. Just prior to peritoneal closure, a 1 inch (2.5 cm.), 20 gage needle was inserted parallel to the abdominal wall under direct vision beside the

TABLE 2.—*Effect of Intraperitoneal Administration of Gases on Adhesions*

Name of Gas	Amount, Cc.	No. of Cases	Incidence of Visceroparietal Adhesions, %	Incidence of Viscerovisceral Adhesions, %
Carbon dioxide.....	300 to 500	3	33½	100 plus
Oxygen.....	300 to 500	3	none	100 plus
Air.....	300 to 500	6	none	100 plus

wound. The peritoneum was closed as described and a wound seal dressing applied without constriction of the abdominal wall.

1. Instillation of Gases (Twelve Procedures). From 300 to 500 cc. of carbon dioxide, oxygen and air, measured by water displacement from a double glass-tubed, rubber-stoppered jar, was instilled immediately after operation through the perforating needle. The injection was stopped as soon as the abdominal wall appeared moderately distended or gas could be detected hissing through the sound seal. The theory of the experiment was based on the principle of pneumothorax; it was hoped that the results would be comparable.

Carbon dioxide was used in three procedures, oxygen in three and filtered air in six. The first gas seemed to absorb in six to eight hours and the second in about nine to twelve hours, but air kept the abdomen somewhat inflated for twenty-four to thirty-six hours.

There was a marked reduction in the incidence of visceroparietal adhesions but no effect on viscerovisceral ones.

2. Instillation of Liquids (Thirty-two Experimental Procedures). Normal isotonic sodium chloride; dextrose, 5 per cent in distilled water; gelatin, 6 per cent and in gel form, and heparin in three forms of solution were employed. On account of the tremendous absorptive

power of the peritoneum, it was decided to test it first in the individual animal and then to attempt to retard it by the use of high molecular weight solutions such as gelatin and finally to employ the fibrin-inhibiting heparin in order to evaluate properly subsequent findings.

As a result of the information previously obtained, the peritoneal incisions were all closed, with careful eversion of the edges and the wounds sealed without constriction.

(a) Isotonic sodium chloride solution was administered immediately after closure through the intra-abdominal needle and subsequently for ninety-six hours in two procedures. Both animals used were kept lightly anesthetized throughout by the addition of small amounts of thiopental sodium to the infusions. Twenty-four hour fluid requirements were estimated on the basis of 20 cc. per pound minimally. Half of the total amount was injected at once and the remainder given by continuous clysis. Further checks on the capacity of the dogs to absorb the fluid were made on the basis of estimates of urinary specific gravity, the average canine variation being from 1.020 to 1.066. It was anticipated that some edema might develop from the excess of chlorides. However, it was thought that this factor might tend to delay peritoneal absorption to some extent.

Preputial edema was noted on the third day of the continuous infusion in 1 animal and on the fourth day in the other. The urinary specific gravity was maintained between 1.010 and 1.028 (indwelling catheter specimens) by administering 40 cc. per pound of isotonic sodium chloride solution (with 0.25 per cent thiopental sodium). Toward the end of the ninety-six hour period signs of pulmonary edema followed shortly by tetanic spasms developed in the first animal, and it died. The second dog was reoperated on nine days later.

In case 1 (post mortem) there were notable edema of all tissues, some free fluid in the peritoneal cavity, slight agglutination between the greater omentum and the small bowel which separated easily on manipulation and no evidence of formed adhesions. The fact that this animal formed no adhesions was not considered too significant, however. The altered metabolism in toxic animals was found to be associated with fibrinolysis on many occasions and will be discussed again.

In case 2 there were no adhesions of the peritoneum of the incision to the viscera. Visceral adhesions, however, recurred 100 per cent.

(b) With the use of the same method, 5 per cent dextrose in distilled water was infused in five procedures. No edema occurred in any of the cases during the ninety-six hour period. Reoperation was performed on the ninth to the fourteenth day. There was a marked reduction in visceroparietal adhesions in all except 1 animal. In this animal pelvic peritonitis developed from a preexisting pyometra, and

of course there were massive adhesions. Viscerovisceral adhesions reformed in all the other cases as well and to a greater extent than before.

It was concluded from these observations that the intraperitoneal infusion of isotonic solutions, with or without the occurrence of tissue edema, did not prevent or inhibit the formation of adhesions *per se*. The reduction in the incidence of visceroparietal adhesions was comparatively the same as could be expected from the utilization of early ambulation, nonconstricting wound dressings and intraperitoneal gases as described before.

(c) Gelatin in 6 per cent solution and in gel form was employed intraperitoneally. Both preparations were made from dehydrated sheet gelatin in distilled water and then sterilized. It was thought that peritoneal absorption would be retarded by a high molecular weight solution for a sufficiently long period to permit healing to occur with possible diminution in extent of adhesions.

Gelatin in 6 per cent solution was administered intraperitoneally to 4 animals by the same method as the fluids described. It was noted that the abdomen in some cases was slightly to moderately distended during the four day period of infusion. Percussion revealed dependent dulness, which could not be elicited when isotonic sodium chloride solution was used. In addition urinary specific gravities remained at a much higher level, varying from 1.032 to 1.050. These observations were indicative of retarded absorption.

Reoperation was performed in twelve to seventeen days.

There was free fluid in the peritoneal cavity in 2 dogs. The amount was, at the most, about 2 ounces (60 cc.), and it appeared similar to ascitic fluid in character. Visceroparietal adhesions were found in 1 case (25 per cent). Viscerovisceral adhesions, though they were seen in all cases, appeared to be reduced about 50 per cent in quantity and in firmness.

These observations would indicate that high molecular weight solutions such as 6 per cent gelatin would tend to combat the formation of visceroparietal as well as viscerovisceral adhesions. This tendency seemed to manifest itself despite the opposing coagulant action of gelatin on blood. Perhaps this effect can be explained on the grounds that the mechanical lubricating fluid action resulting from retarded peritoneal absorption, assisted by peristalsis, counteracts to a certain degree the normal agglutinating tendency of gelatin to precipitate fibrin, a precursor of adhesions. The following experiments in which gelatin gel was used and an opposite effect obtained would seem to bear this out.

In four procedures gelatin gel (25 per cent in distilled water), 100 cc., was applied to all raw surfaces just prior to closing the peritoneum. No infusions were given. In 1 animal severe gastroenteritis developed

twenty-four hours postoperatively, and it died four days later from wound dehiscence with evisceration. In this case there was a minimum of adhesions, but there was also poor healing just as in other animals dying in toxemia and shock.

The findings here could not be regarded as having any special bearing on the problem since reoperation revealed reformation of viscerovisceral and visceroparietal adhesions in all of the other 3 dogs. It was noted that the gelatin had been completely absorbed and that despite the known clotting action of this substance there was apparently no pronounced increase in adhesions over what would otherwise be expected.

(d) Heparin in three types of solution was infused intraperitoneally in seventeen procedures. Isotonic sodium chloride solution was used as a vehicle in three, 20 per cent gelatin in seven and Pitkin's menstruum in seven.

Heparin in isotonic sodium chloride solution was given after operation by the method of Lehman and Boys to 3 animals selected because they were known to have massive adhesions. Two of these dogs had been operated on three times and 1 four times. Three hundred cubic centimeters of isotonic sodium chloride solution containing 10,000 units of heparin was introduced intraperitoneally immediately after operation. Twelve hours later 5,000 units in 300 cc. of sodium chloride solution was given, and this was repeated every twelve hours until 40,000 units of heparin had been administered over a seventy-two hour period.

Coagulation time was checked by the Lee and White method at varying intervals after each infusion. Each time 1 or 2 cc. was aspirated through the intraperitoneal needle and observed for evidence of intraperitoneal bleeding. Two sets of observations were made.

1. After the first infusion, the blood coagulation curve varied from a low of 8 minutes to a peak of 19 minutes (the normal canine coagulation time being 6 to 8 minutes). This peak was attained in from two to two and a half hours after the infusion, and the value returned to normal in an average of about five hours.

After subsequent infusions using half the amounts of heparin, the blood coagulation curve rose to a high point of 13 minutes in about two hours and returned to normal in about four hours. There was apparently no residual or cumulative effect from the preceding administration of heparin.

The periods of decreased clotting were therefore of five and four hours' duration respectively, alternating with periods of normal coagulation of seven and eight hours.

2. Peritoneal fluid could be aspirated for the first two hours only because of the rapidity of absorption. The peritoneal cavity was therefore subsequently irrigated with 100 cc. of isotonic sodium chloride.

solution at four hour intervals to check for bleeding. A Talqvist chart was used as a standard of comparison. It had been previously determined that after standard operative procedures one might expect a normal serosanguineous exudate color of about 10 per cent on the chart after irrigation with 100 cc. of sodium chloride solution during the first twenty-four hours in most cases. Therefore, any color intensity exceeding that in the irrigation returns was taken to be a proportionate estimate of bleeding.

Reoperation after healing of the wound gave the following findings: Visceroparietal adhesions were definitely reduced. One animal had none, and the other 2 had slight adhesions to the incision or to the area that had been perforated for the infusions. Viscerovisceral adhesions were definitely reduced to about half of what could normally be anticipated. In addition the adhesions found were longer and more tenuous and elastic than before.

Peritoneal aspirations revealed slight to moderate bleeding in all cases two hours after the initial large dose of heparin. In no case, however, did the color reading exceed 40 per cent on the Talqvist chart. Even when bleeding was noted after the subsequent infusions with adjusted dosage, it seemed to decrease gradually so that from six to eight hours postoperatively the color was practically normal.

The fact that some oozing did occur did not affect the findings. Apparently heparinized blood differs from normal to the extent that it is absorbed from the peritoneal cavity without contributing to the formation of adhesions.

Heparin in 20 per cent gelatin was used in seven procedures. It was thought that gelatin might serve to retard the liberation of heparin and afford a method of simplification of the method described before. (These experiments were performed prior to the reported successful use of Pitkin's menstruum as a vehicle in the literature). It may be noted in passing that heparin added to relatively viscous gelatin seems to increase its fluidity, facilitating its administration through a medium gage hypodermic needle.

Total preliminary dosage was calculated on the basis of 3 mg. (or 0.33 cc.) per pound on a twenty-four hour schedule. This amount of heparin in 10 cc. of 20 per cent gelatin was applied to the traumatized areas of peritoneum immediately after operation by paracentesis. The abdomens were gently kneaded to spread the medication. Four hours later, blood coagulation times were checked by the capillary tube method. If the coagulation time was less than 15 minutes, an additional proportionate amount of the same preparation was given.

The revised estimated dosage of heparin in gelatin was then reinjected at twenty-four hour intervals for a total of ninety-six hours in the same manner. Blood coagulation times were then taken at twelve

4 of the cases. In 1 instance a loop of ileum was partially obstructed by an adhesive band. Visceral adhesions were also found in greater amounts. The general nature of the adhesions was similar to that seen in other heparinization procedures, although they were thinner, more tenuous and more elastic than those ordinarily found. It was believed that the greater irritation of the peritoneal endothelium by the menstruum somewhat counteracted the fibrolytic action of the anticoagulant.

Despite careful hemostasis, capillary oozing even to the extent of mild intraperitoneal hemorrhage was frequent. However, this appeared to be self compensated by the rapid absorption of heparinized blood by the peritoneum. The blood hemoglobin content returned to normal shortly after termination of the heparinization. It is possible that the heparinized blood itself acts as a vehicle for the prolongation of action of the anticoagulant.

The finding of Laufman and Heller that heparinization did not interfere with healing of the wound could be corroborated. All wounds were healed by the seventh day except in the cases in which infection occurred. There was only 1 case of wound dehiscence, and that occurred in a toxic animal. Although the wounds appeared to contain less fibrin, the growth of fibroblasts was apparently not impeded.

## PART TWO

In view of the encouraging findings noted, it was decided to investigate the relative merits of administering heparin and dicumarol systemically in the attempt to inhibit the formation of postoperative adhesions. Certainly, if fibrin was the determining factor it seemed to be, then the retardation of its formation by the use of anticoagulants, by whatever route administered, should also be effective.

Accordingly, 24 dogs were subjected to a total of sixty-four experimental procedures to test the plausibility of this assumption.

Since Hertzler and others had already proved that all potential adhesions are evident by the fourth day after operation, a treatment period of ninety-six hours was again chosen. The technical details of early ambulation, careful peritoneal eversion in wound closure and noncompressing wound dressings, all having shown promise of being helpful, were also employed.

It was decided to administer heparin subcutaneously in Pitkin's vehicle and in 20 per cent gelatin, because this was most convenient and had been proved to be as efficacious as when given intravenously. Dicumarol was given orally in tablet form.

Preliminary procedures for the production of adhesions were repeated according to the method described. To assay the relative incidence of adhesions in the upper (supramesocolic) and lower

(inframesocolic) portions of the abdomen, as well as to study the relative tendencies of denuded and traumatized surfaces to adhere, a small area of serosa was dissected off and another larger area abraded in the upper as well as the lower portion of each dog's abdomen.

The work was subdivided into experiments on four groups of 16 animals each.

1. Heparin suspended in Pitkin's menstruum was used in the first group.

2. Heparin in 20 per cent gelatin was used in the second group.

3. Dicumarol was used orally in the third group.

4. A combination of heparin and dicumarol was employed in the last group of 16.

Group 1. Heparin in Pitkin's base was given subcutaneously in preestimated doses of 2 mg. per pound (0.5 cc. or 50 mg. per 25 pounds [11.3 Kg.]). No vasoconstrictors were employed. The first dose was injected one hour after the completion of the preliminary celiotomy. This interval was selected for two reasons: first, because it takes from one to two hours for the anticoagulant action to manifest itself by this method, and, secondly, this would permit enough time to elapse for firm clot retraction in order to minimize postoperative hemorrhage.

Blood coagulation times were checked at four hour periods for the first twenty-four hours and whenever indicated subsequently in an attempt to maintain the coagulation time at 15 minutes or over. The capillary tube method was used since this was less time consuming and easier to perform as well as being sufficiently accurate for all practical purposes.

Supplementary injections were given when indicated during the first day. Again it was found that proportionately smaller doses were required on the second, third and fourth days to maintain the necessary prolongation of coagulation, indicating that the duration of effect was over twenty-four hours. By calculating and comparing dosages, it was found that the average duration of action of heparin in Pitkin's vehicle was thirty-seven hours.

For the preliminary celiotomy in all the procedures in this part of the investigation a 5 inch (12.7 cm.) incision was made through the linea alba extending up to about 3 inches (7.6 cm.) below the xiphoid to avoid the peritoneal reflection over the falciform ligament of the liver. The serosa was denuded and abraded on the anterior aspect of the stomach and on a loop of small bowel. Just prior to closure a short piece of ureteral catheter was inserted into the abdomen through a stab wound for periodic irrigation to test for possible hemorrhage. The abdomen was then closed according to the manner described previously.



It was noted that a wide variation in coagulation times occurred, especially during the first twenty-four hours on an estimated dosage of 2 mg. per pound, the range being from 10 minutes up to 45 minutes. Several factors were thought to be responsible for this: first, the individual differences in speed of absorption; second, variations in the total amounts of the preclotting elements such as prothrombin, ionic calcium, thrombokinese, vitamin K and autogenous heparin, and, finally, variable hepatic function in the metabolism of these substances. Subsequent dosages were individually adjusted to give a final average deviation in coagulation times of 14 to 31 minutes for the ninety-six hour period.

Irrigations through the indwelling ureteral catheter with 100 cc. of isotonic sodium chloride solution were performed at four and eight hour intervals to test for hemorrhage. It was observed that little bleeding occurred by this method compared to the intraperitoneal administration of the same drug. In only 2 instances did the color chart readings exceed 20 per cent, and then only slightly. The coagulation times in these dogs were over 40 minutes at the time.

On reoperation after ten to twelve days the following observations were made: In 3 dogs hematomas had developed around the indwelling catheters. This was probably due to the fact that in these cases the perforation had been made through muscle, since none of the other animals with midline (fascial) punctures exhibited this complication.

Visceroparietal adhesions were found in 2 cases, an incidence of 12 per cent. In both instances the greater omentum was wrapped around the catheter and was slightly adherent to the adjacent peritoneal wound. In 1 a small pledget of gauze had been accidentally left in the abdominal cavity at a former operation and was found encapsulated in a large mass of omentum adherent to the uterus.

Visceral adhesions occurred in 9 instances, or 56 per cent. Practically all were limited to the denuded areas of stomach and small bowel. Omentum, other loops of bowel or falciform ligament was seen adherent to these spots. The adhesions were thinner, more elastic and more easily separable than would normally be expected, however, and no potentially obstructive kinks or bands could be found. The frequency of upper or lower abdominal adhesions to raw areas was about equal. No adherence of the areas of stomach or bowel which had been merely abraded was observed, although in 2 cases a long marker suture was enmeshed in other adhesions.

Review of the coagulation times indicated that the frequency of adhesions varied almost directly with the extent of prolongation of this factor inasmuch as the animals with no adhesions had a coagulation time of over 27 minutes, especially during the first twenty-four hours. In

the other 9 instances the clotting times were from 10 to 18 minutes the first day and from 14 to 35 minutes subsequently. It is apparent that the maximum prolongation of blood coagulation within the limits of safety during the first twenty-four hours gave the best results.

Postoperative hemorrhage did not occur with this method, probably for several reasons. With careful hemostasis and enough time lapse for firm clot retraction prior to heparinization, the increased blood fluidity offered no hazard in a closed vascular system. It is known that formed thrombus and capillary permeability are not altered by anti-coagulants.

Group 2. Sixteen experiments were conducted with heparin in 20 per cent gelatin administered subcutaneously. The same method of procedure and dosage schedules as that used in group 1 was fol-

TABLE 4.—*Use of Heparin in Pitkin's Vehicle Subcutaneously*

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Dosage
Preliminary, 2 mg. per pound; subsequent, in proportion to fluctuation in coagulation time
Duration of effect—average, 37 hours
Number of procedures—16
Coagulation times
First 24 hours, from 10 to 45 minutes; average over the 96 hour period, from 18 to 31 minutes.
Incidence of bleeding
Hematomas—Intramuscular, 3 cases, or 18 per cent
Intraperitoneal oozing—2 cases, or 12 per cent
Frank hemorrhage—none
Findings
Adhesions markedly reduced; directly proportional to extent of prolongation of coagulation times especially during the first 24 hours; visceroparietal adhesions occurred in only 12 per cent; viscerovisceral adhesions seen in only 50 per cent of animals with denuded serosas and in less than 1 per cent of the others

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lowed. Greater care, however, was taken to place the piece of ureteral catheter through a fascial perforation and to fix the intra-abdominal tip by a suture in such a way as to permit minimal projection beyond the peritoneum.

As was expected, the findings in general were similar to those in group 1. The main difference noted was in the relative ability of the plain gelatin to retard heparin absorption in comparison to Pitkin's menstruum. Quantity for quantity, the latter is somewhat more efficient. Repeated checks of coagulation time indicated that the average duration of effect of heparin in gelatin was from eighteen to twenty-five hours and that the average variation for the ninety-six hour period was from 7 to 42 minutes for the entire group.

Only in 1 dog did a mural hematoma develop around the indwelling catheter and 2 animals showed evidence of frank intra-abdominal hemorrhage when the coagulation time was 23 and 38 minutes respectively.

Visceroparietal adhesions were found in 2 instances; in 1 they were between a denuded area of jejunum and the peritoneum in the area of the perforating catheter, and in the other the denuded area on the stomach and the upper end of the peritoneal incision were agglutinated together.

Viscerovisceral adhesions occurred in 11 cases, or 68 per cent, mainly between raw surfaces and contiguous omentum. Where the serosa had been abraded only, adhesions were found in 2 instances, or 12 per cent.

Group 3. Dicumarol was given orally to an experimental group of 16 dogs in which adhesions were known to have formed in previous experiments. The first dose of the drug was administered twenty-four hours preoperatively in each instance on the basis of 2 mg. per pound. Subsequently, 0.5 to 4 mg. per pound every twenty-four hours was given over a four day period.

TABLE 5.—*Use of Heparin in 20 Per Cent Gelatin Subcutaneously*

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Dosage—same as in table 4
Duration of effect—average, 21 hours
Number of procedures—16
Coagulation times
Variation from 7 to 42 minutes for the 96 hour period.
Incidence of bleeding
Hematomas—1 case (less than 1 per cent)
Intraperitoneal hemorrhage—2 cases, or 12 per cent
Findings
Adhesions markedly reduced as before; visceroparietal adhesions occurred in 12 per cent (only in denuded areas); viscerovisceral adhesions occurred in 68 per cent in denuded places and only in 12 per cent in other areas

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In half of this group it was decided to test the influence of hepatic function on prothrombin time and dicumarol action by using chloroform as the anesthetic during the operation and for a variable time up to an hour afterward. In the remaining 8 cases the method of anesthesia used previously was repeated.

Since all the animals had already been subjected to at least one midline celiotomy, it was necessary to use right or left rectus incisions. The muscles were retracted laterally in each case rather than split in order to minimize bleeding. Ureteral catheters were introduced as before to serve as tap indicators for possible bleeding.

Prothrombin times were determined every twenty-four hours by the method of Quick and plasma prothrombin concentration noted in percentage of normal. Great difficulty attended the subsequent administration of dicumarol because of the wide variations and sudden fluctuations in these calculations of prothrombin time. Several preparations of the thromboplastin solutions used in the tests were tried, but these

differences persisted notwithstanding. It was found that the average prothrombin time was 5 to 7 seconds and that bleeding did not occur until it was prolonged over 32 seconds; in human beings the normal plasma prothrombin time is 15 seconds and bleeding can be expected when it exceeds 25 seconds.

The chloroform-anesthetized animals required much smaller subsequent dosages of the drug, and their prothrombin times were easier to control than those of the other dogs. This was indication of hepatic damage, since it is known that bleeding in jaundice is due to increased prothrombin time. Daily repeat doses varied from 0.5 to 1.5 mg. per pound in this group to maintain a plasma prothrombin concentration below 30 per cent of normal (also the critical figure used in anti-thrombosis therapy).

The remaining 8 dogs in this group required from 2 to 4 mg. per pound per day to maintain a similar prothrombin plasma level. This appears to indicate that dogs have several times as much prothrombin in their plasma as human beings, since the effect of dicumarol is cumulative and additive and clinical experience has shown that, proportionately, one third to one fifth as much of the drug is required to maintain this level in the latter species.

The mean prothrombin concentrations for the ninety-six hour period was from 0 per cent to 45 per cent of normal for the entire group. Bleeding occurred whenever the plasma concentration of this protein was below 5 per cent. Four animals died of uncontrollable intraperitoneal hemorrhage, 1 on the second day, 2 on the third day and 1 on the fourth day. The prothrombin levels in these animals before death were all at or near zero. Large doses of vitamin K were ineffective in checking the bleeding. Three additional dogs showed signs of intra-abdominal oozing and hematomas of the wound. These were of minor degree and relatively self limited and compensated.

Postmortem examination of the 4 animals dying of hemorrhage and shock revealed a minimal amount of visceral and parietal adhesions. None of the abraded areas appeared to be involved. In 2 instances the omentum was agglutinated to the denuded areas on the stomach. It seemed from the localization of the hematomas that hemostasis after denudation in these 2 cases had been inadequate.

The remaining 12 dogs were reoperated on after nine to twelve days. Visceroparietal adhesions were seen in 4 animals. In 1 the raw areas on the stomach, the greater omentum and the transverse colon were agglutinated together in one large mass at the upper angle of the incision. In the other 3 cases raw areas of stomach and bowel were implicated.

Visceral adhesions occurred in 8 instances, or 50 per cent. The attachments appeared as bulky edematous agglutinations, in contra-

distinction to the tenuous veluminous attachments seen when heparin was used. Again the denuded areas were mostly involved, although in 1 dog three loops of small bowel were attached to the uterus and adnexa while the denuded area of bowel was sealed with greater omentum.

It was the general impression that dicumarol was far inferior to heparin as an agent for the prevention of adhesions. Control of dosage in experimental animals was much more difficult. Laboratory procedures for checking dosage were more cumbersome also. The incidence of hemorrhage, partly because of these factors, was much more common and of much more serious importance. Finally, the occurrence of adhesions was considerably greater with dicumarol than with heparin.

Group 4. Heparin and dicumarol in combination were administered in sixteen procedures.

TABLE 6.—*Oral Administration of Dicumarol in Prevention of Adhesions*

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Dosage
Initial, 2 mg. per pound; subsequent, every 24 hours 0.5 to 4 mg. per pound
Number of procedures—16
Prothrombin concentration fluctuations—0 to 45 of normal
Incidence of bleeding
Hemorrhage—fatal in 4 animals, or 25 per cent; compensated in 3, or 18 per cent
Findings
Adhesions moderately reduced; visceroparietal adhesions found in 6 dogs, or 37 per cent; viscerovisceral adhesions found in 8 dogs, or 50 per cent (most adhesions occurred in connection with denuded areas)

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The dicumarol was first given twenty-four hours before operation in amounts of 2 mg. per pound. This produced an average prothrombin time of 45 to 60 per cent of normal. The antifibrin effect was then exerted by injecting heparin in Pitkin's menstruum immediately after the incision was closed in the same dosage as had been used before, i. e., 2 mg. per pound. Anticoagulation was maintained by daily feeding of dicumarol in amounts of 2 to 4 mg. per pound checked against prothrombin concentrations.

The investigations were carried on by the same method used before. All the animals in this group had been operated on at least once and some three or four times. Their propensity for forming adhesions was a matter of record, so that fairly accurate conclusions could be drawn as to the efficacy of the experiments in preventing them.

The average prothrombin concentration for the entire group for the four day period was from 0 to 50 per cent of normal. Coagulation times checked twenty-four hours after the administration of heparin in Pitkin's menstruum ranged from 12 to 29 minutes.

Three animals died. One died on the fourth day from hemorrhage and shock, in another a large hematoma had developed in the incision on the third day and evisceration occurred on the sixth, and the third died in hyperpyrexia on the seventh day of an undiagnosed pathologic process. Postmortem examinations were performed on these animals and significant findings noted.

The other 13 dogs were reopened a week to ten days later and explored. In general, the observations made in the preceding set of experiments were reaffirmed. No material differences in the nature or extent of adhesions as a result of the heparin effect exerted over a twenty-four hour period could be seen. Although the adhesions in many instances appeared to possess greater transparency and tenuity, their appearance was not nearly as remarkable as when heparin alone

TABLE 7.—*Administration of Heparin Subcutaneously and Dicumarol Orally for Adhesions*

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Dosage

Heparin in Pitkin's base, one injection immediately after closure on basis of 2 mg. per pound

Dicumarol, first dose on basis of 2 mg. per pound started 24 hours pre-operatively, with subsequent doses of 2 to 4 mg. per pound every 24 hours

Number of procedures—16

Prothrombin concentration variations—0 to 50 per cent of normal

Coagulation time variations—12 to 29 minutes

Complications

Three deaths; cause of 1 unknown, 2 from shock and hemorrhage (one of the dogs eviscerated)

Findings

Adhesions moderately reduced; visceroparietal adhesions noted in 5 cases, or 31 per cent; viscerovisceral adhesions noted in 9 cases, or 56 per cent

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was used over the longer period. Dicumarol seems to further the formation of bulky edematous agglutinations.

Visceroparietal adhesions were found in 5 animals, or 31 per cent. Viscerovisceral agglutinations occurred in 9 animals, or 56 per cent.

#### COMMENT

Granted that the formation of postoperative adhesions is simply one aspect of the natural salutary process of repair, the relative frequency of pathologic sequelae intensifies the important significance of any agent or agents capable of limiting the extent of this process. The connective tissue cells which react to injury are the fibrocytes and the macrophages (histiocytes). Granulation tissue is produced by an ingrowth of fibroblasts and buds of endothelial cells into the exudate, producing a highly vascularized mass. As organization proceeds to completion, the connective tissue contracts with the deposition of collagen, and the capillaries decrease in size and number and mostly disappear, leaving dense pale scars or bands. Organization of fibrinous exudates between opposing serous surfaces results in adhesions. Utilization of

agents or methods that keep these surfaces apart or decrease the amount of fibrin present tends to prevent adhesion and does not impede normal healing in areas operated on.

The fact that adhesions failed to appear in toxic or dying animals had been noted on several occasions. Tagnon and others have shown that fibrinolysis occurs in such cases and that if blood is taken in a test tube without an anticoagulant and allowed to clot it is observed that the clot disappears in a short time and becomes fluid again. Moreover, it cannot be clotted again by the addition of thrombin because the blood no longer contains fibrin. In Russia, during the war, it was found that blood taken from soldiers who died suddenly could be stored without the addition of an anticoagulant for the same reason.

In general, it is much easier to prevent partially the formation of adhesions between the parietal and visceral peritoneal layers than between contiguous visceral serosae. The principle of peritonealization of all raw surfaces and the avoidance of surgical trauma is obviously of critical importance. Careful eversion of incised peritoneal edges and the method of suturing employed to effect this is the corollary of this principle. Early ambulation and wound dressings that do not compress the abdominal wall to the operative areas are definite factors. Finally, the interposition of gases and poorly absorbed solutions between the viscera and the abdominal wall tends to decrease adhesion between these layers.

To prevent the pathologic agglutination of the greater omentum to viscera with serosal injury is a far greater problem. The crucial consideration, however, seems to be the local concentration of fibrin, which as it clots forms the bridges through which fibroblasts permeate during the process of organization. The relative concentration of the other blood-clotting elements such as ionic calcium, thrombokinase, vitamin K and autogenous heparin and of prothrombin and thrombin, the precursors of fibrinogen and fibrin, is directly related to hepatic function and probably accounts for the variable tendency of adhesions to form in different subjects.

The introduction of the anticoagulants, especially heparin, intraperitoneally or systemically soon after serosal trauma diminishes the volume of fibrin in the exudate and so tends to limit the formation of local adhesions. For the same reason any adhesions that do form are more tenuous and elastic and therefore less likely to cause complications. The systemic use of anticoagulants for this purpose has been found to be more practical and more effective as well as less hazardous. Pitkin's menstruum and 20 per cent gelatin are good vehicles for heparin, although the former is considerably more irritating and painful locally.

The danger of hemorrhage, though real, should not be too great a deterrent, provided ordinary precautions are observed. Attention to hemostasis, postoperative coagulation and prothrombin times, as well as clinical observations of the pulse, blood pressure and blood counts, over a period of four to five days mitigates against this complication. The effect of heparin administered in short-acting vehicles for the first twenty-four hours is readily controllable. Excessive lowering of the clotting time is combated by transfusion, and Allen and others have shown that large doses of synthetic vitamin K intravenously are remedial against too great a reduction in plasma prothrombin. The action of dicumarol in experimental animals has been found much more difficult to control and the incidence of serious hemorrhage much more frequent than when heparin alone was employed. Furthermore, dicumarol is inferior to heparin as an antiadhesions agent.

#### SUMMARY AND CONCLUSIONS

1. In part I of an experiment 37 dogs were subjected to one hundred and eight procedures in an attempt to control postoperative adhesions by transperitoneal or intraperitoneal operations and the following observations made: Early ambulation, careful peritonealization of raw surfaces, eversion of peritoneum by interrupted sutures in closures, avoidance of compressing wound dressings, pneumoperitoneum and infusions of slowly absorbed solutions such as gelatin were all partly effective in reducing the incidence of visceroparietal adhesions, despite the fact that viscerovisceral adhesions recurred 100 per cent and more.

To combat the latter, infusions of heparin in isotonic sodium chloride solution, in 20 per cent gelatin and in Pitkin's menstruum were employed, and a reduction of from 50 to 75 per cent was obtained. In these experiments, best results were secured with 20 per cent gelatin as a vehicle. This decrement affected both visceroparietal and viscerovisceral adhesions. The chief complication was intraperitoneal bleeding, but this was largely self compensatory by absorption in practically all cases, the hemoglobin content returning to within 10 per cent of normal by the fourth day postoperatively. The least amount of bleeding occurred when gelatin was used as a menstruum.

2. In part II heparin and dicumarol were given systemically alone and in combination in sixty-four experimental procedures, divided into four groups. In these cases areas of serosa were not only abraded but also denuded. The results were as follows:

Group 1 (heparin in Pitkin's vehicle), Visceroparietal adhesions occurred in only 12 per cent. Viscerovisceral adhesions occurred between abraded areas in less than 1 per cent and in denuded areas in only 56 per cent.



Group 2 (heparin in 20 per cent gelatin). Visceroparietal adhiscence was found in 12 per cent and viscerovisceral adhiscence between abraded areas in 12 per cent and in denuded areas in only 68 per cent.

Group 3 (dicumarol orally). Visceroparietal adhesions were seen in 37 per cent and viscerovisceral adhesions in 50 per cent (mostly in connection with denuded surfaces. Fatal hemorrhages occurred in 4 of 16 animals (25 per cent). This drug was exceedingly difficult to control in dosage and action.

Group 4 (dicumarol orally and heparin in Pitkin's base administered subcutaneously). Visceroparietal adhiscence was seen in 31 per cent and viscerovisceral adhiscence in 56 per cent. Fatal hemorrhage occurred in 2 animals (12 per cent).

Heparin administered systemically by the subcutaneous route is a practical, effective and relatively safe agent in reducing the incidence of postoperative adhesions in experimental animals. It is more effective when used this way than when infused intraperitoneally, because its duration of action is more constantly sustained. Heparin is more effective and controllable than dicumarol or dicumarol and heparin in combination when used in the manner described. The hazard of serious hemorrhage is much less as well. Its action may be enhanced by utilizing some of the measures described here.

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## EFFECT OF OXIDIZED CELLULOSE IN THE PROTECTION OF THE SUTURE LINE IN INTESTINAL ANASTOMOSES IN DOGS

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**L**EAKAGE from the suture line in intestinal anastomoses is a complication of the gravest nature. Since oxidized cellulose, an absorbable substance that can be left in the tissues, has been introduced into surgical practice, its value as a protective aid in intestinal anastomoses seemed worthy of investigation.

The literature on intestinal anastomoses has been extremely voluminous.<sup>1</sup> The fundamental work of Lembert<sup>2</sup> and Halsted,<sup>3</sup> insisting on the importance of the serosal and submucosal sutures, remains the basis of successful anastomoses of the bowel.

As revealed by a rather extensive search of the literature,<sup>1</sup> the use of materials in protection of the anastomotic suture line apparently has not been reported to any great extent. Freeman<sup>4</sup> suggested the use of omental grafts for this purpose; Fenton and Peet<sup>5</sup> reported on the use of omental grafts in intestinal anastomoses in dogs. Devine<sup>6</sup> presented a preliminary report in which he used peritoneal and split thickness grafts applied with fibrin fixation to the anastomotic suture line in dogs.

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Kenyon and his associates<sup>7</sup> found that oxidation of cellulose in a closed chamber with nitrogen dioxide produced an absorbable material. Its physical and chemical properties, as well as its clinical applications, have been extensively investigated and reported in the literature.<sup>8</sup>

Burns<sup>9</sup> found that oxidized cellulose implanted in the various portions of the peritoneal cavity of dogs forms a brownish gelatinous mass which gradually decreases in size until complete absorption occurs. Dmytryk,<sup>10</sup> working with dogs whose peritoneum had been traumatized, found that the primary reaction of the tissues to oxidized cellulose was a fibroplastic proliferation, with the formation of adhesions between omentum and intestines. When the oxidized cellulose was applied immediately after the incidence of the trauma, the adhesions were finer and less numerous than in the controls.

In the healing of serosal wounds, Hertzler<sup>11</sup> stated that within a few minutes the angle between the apposed surfaces is filled with a clear structureless exudate in which fibrin bundles rapidly form. With the passage of time, these bundles form fibrous tissue, cells wandering between the interstices of the fibrin bundles without replacement of the latter.

With these observations in mind, the following experiments were set up to investigate the possibility of oxidized cellulose protecting the anastomotic suture line. Two series of experiments were performed.

In both series adult dogs of various sizes and both sexes were used. Preoperative medication with morphine sulfate was used in doses regulated by the size of the animals. Anesthesia was induced and maintained by the intravenous injection of pentobarbital sodium. Strict aseptic technic was used in all the procedures. The abdominal wall was shaved and treated with tincture of iodine prior to the incision of the skin.

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In series I the abdomen was opened by a right rectus incision. The rectus muscle was split, and the peritoneal cavity was entered. The ascending colon was identified and brought to the surface. The peritoneal cavity was protected by sterile sponges. After the colonic contents were stripped from the segment of bowel to be used, the colon was clamped by rubber-covered intestinal forceps. The colon was then transected at a point 8 to 10 cm. from the ileocecal junction and immediately anastomosed end to end with a continuous circular through-and-through suture of the bowel. In the controls the abdominal wall was then closed in layers without drainage. Cotton was used as suture material throughout. A collodion covering was placed over the skin sutures.

The experimental animals were subjected to an identical procedure, with the additional step of applying an eight-ply layer of oxidized cellulose to the anastomotic suture line. The oxidized cellulose was held in position by interrupted serosal sutures placed well away from the line of intestinal suture. Great care was exercised that the lumen of the bowel was not entered by these supporting sutures.

In series II the steps of opening the abdomen, isolating the colon and protecting the peritoneal cavity were identical with those in series I. The colonic contents were stripped from the portion of the bowel to be used; the bowel was clasped with rubber-covered intestinal forceps and was transected. The cut ends were then approximated by the insertion of a Maunsell mesenteric suture, followed by a through-and-through continuous mucosal suture. The serosa was approximated by a serosal suture of the Cushing type. The abdominal wall was closed in layers. Cotton was used throughout as the suture material.

In the experimental animals of series II an identical procedure was performed with this additional step: After the two layer anastomosis had been done, an eight-ply layer of oxidized cellulose was put about the anastomotic line and held in position by interrupted serosal sutures placed well away from the line of anastomosis, care being exercised that the lumen of the colon was not entered in placing these sutures. The abdominal wall was closed in layers as in the previous operations, and the skin incision protected with collodion. Cotton was used throughout as the suture material.

After these described procedures, the animals were placed in cages and their progress observed daily. Water and food were allowed as tolerated, and no special animal diets were used.

#### RESULTS

In series I, 3 dogs were used as controls. Two of these animals died, 1 at the end of twenty-four hours and the other at the end of forty-eight hours. One animal survived for ninety-six hours and was then killed.

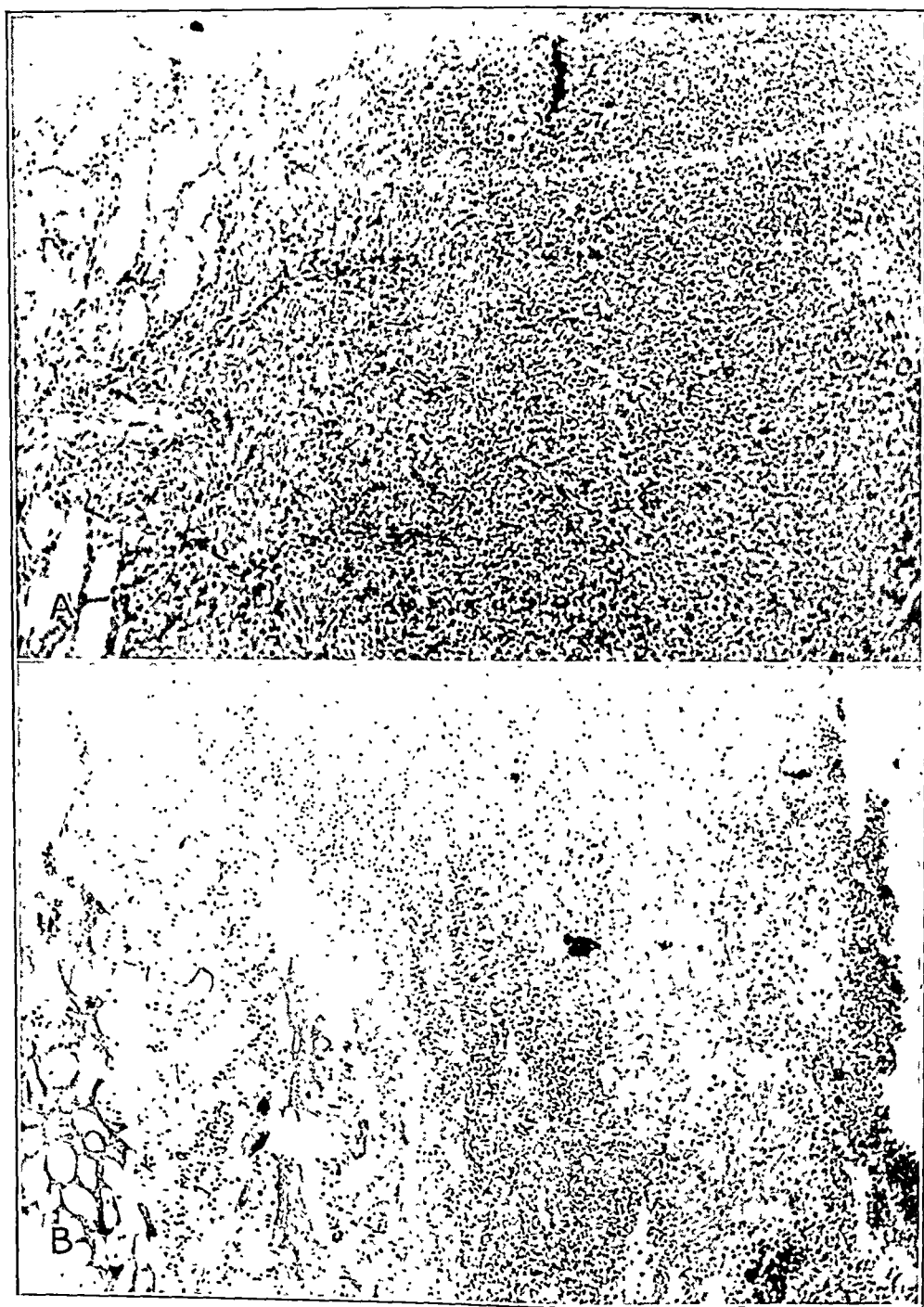


Fig. 1.—*A*, section of colon, showing acute inflammatory reaction with polymorphonuclear cell infiltration in serosal layer in a control animal in series I. Hematoxylin and eosin stain;  $\times 100$ . *B*, section of colon showing acute inflammatory reaction in bowel wall. Fragments of oxidized cellulose in serosa of bowel with surrounding inflammatory exudate. Experimental animal in series I. Hematoxylin and eosin stain;  $\times 100$ .

At autopsy the first 2 animals showed a generalized purulent peritonitis, with ileus. A large amount of free hemorrhagic exudate was found in the peritoneal cavity. The omentum was edematous and the colon gangrenous. No attempt at healing of the anastomotic line was evident, as there was free escape of colonic contents through the line of anastomosis. Histologically, a diffuse inflammatory exudate was present through the entire bowel wall, with gangrenous changes in the line of anastomosis. Much edema and many acute inflammatory cells were present in these sections. Few bacteria were noted in the exudate. Figure 1*A* is a photomicrograph showing these changes.

The animal killed at the end of ninety-six hours showed localized peritonitis, with many adhesions between the omentum, ileum and colon. No free fluid was found in the peritoneal cavity. There was little evidence of healing of the anastomotic line. Histologically, there was much serosal purulent exudate with a few clumps of bacteria. Early granulation tissue was present with a few foreign body giant cells about the cotton suture material. Much edema of the tissues was noted.

In the experimental group of series I the suture line was protected by an eight-ply layer of oxidized cellulose. Of this group, 3 animals died at the end of twenty-four hours, 1 died at the end of forty-eight hours and 1 lived five days.

Autopsy on the 4 animals that lived for twenty-four hours and forty-eight hours respectively showed acute purulent peritonitis with edema and gangrene of the colon. Much free hemorrhagic exudate was present. No healing of the line of anastomosis was present. Fecal material escaped from the lumen of the bowel between the sutured ends. In 3 of the animals no gross evidence of oxidized cellulose was found; in 1 animal that lived twenty-four hours postoperatively only a few scattered shreds of oxidized cellulose were found adherent to the serosal surface of the colon.

Histologically, a diffuse inflammatory exudate was seen throughout the bowel wall with a serofibrinous exudate on the serosa. Microscopic patches of oxidized cellulose were seen in which were many bacteria. More inflammatory cells were noted in the margins of the oxidized cellulose patches. Thrombi were present in many of the veins. Figure 1*B* is a photomicrograph showing the changes as described. Figure 2*A* is a higher power photomicrograph showing the particles of oxidized cellulose with the clumps of bacteria in and about the oxidized cellulose, with the acute inflammatory cells and hemorrhagic exudate. Figure 2*B* is a high power photograph of the bacteria and particles of oxidized cellulose.

Evisceration occurred in the animal surviving five days, and it was killed. There were many adhesions between colon, ileum and omentum, with localized peritonitis. Healing of the line of anastomosis was

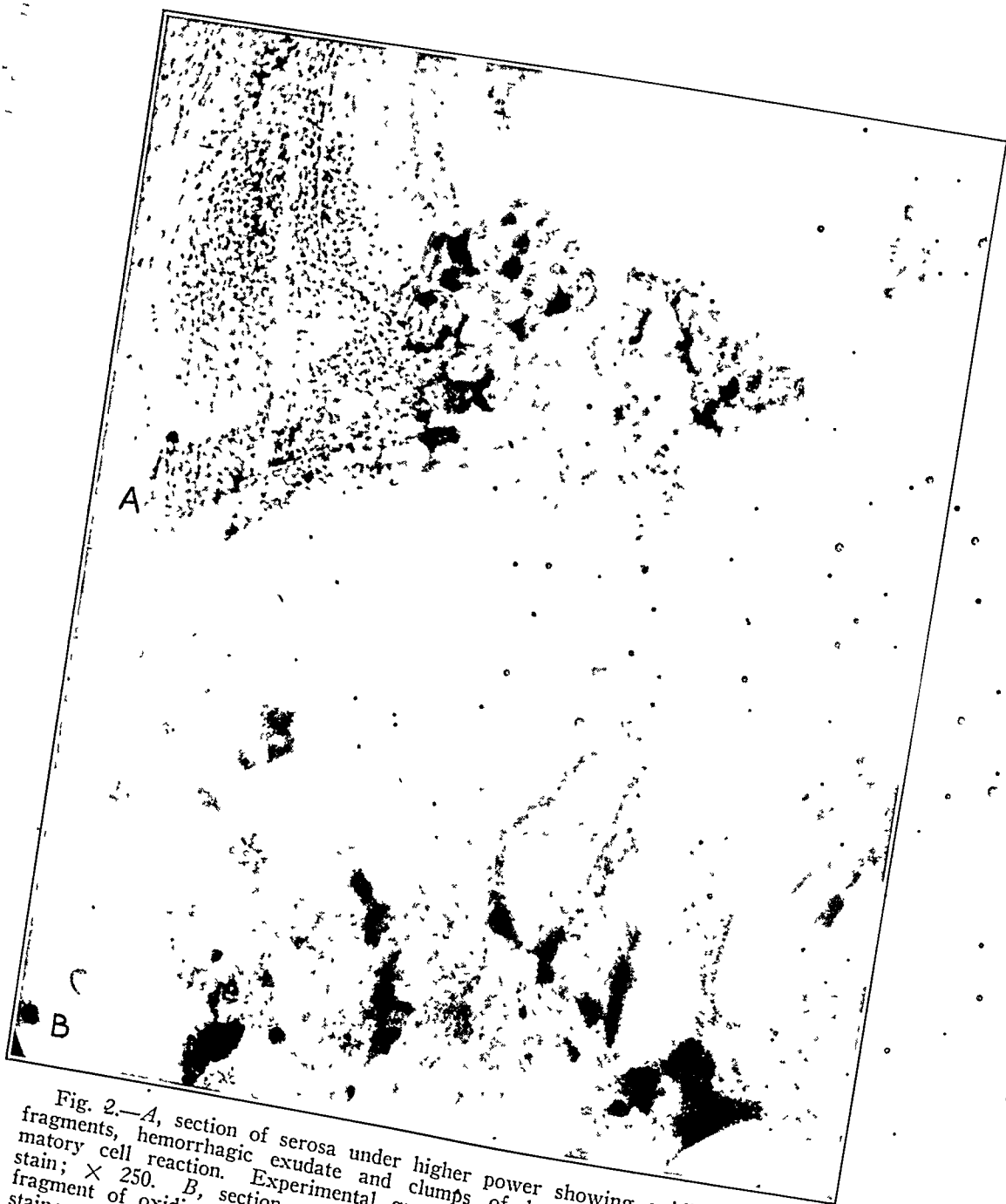


Fig. 2.—*A*, section of serosa under higher power showing oxidized cellulose fragments, hemorrhagic exudate and clumps of bacteria with acute inflammatory cell reaction. Experimental group, series I. Hematoxylin and eosin stain;  $\times 250$ . *B*, section under high power showing hemorrhagic exudate, fragment of oxidized cellulose and clumps of bacteria. Hematoxylin and eosin stain;  $\times 430$ .





Fig. 3.—*A*, section of colon, showing clean serosa with chronic inflammatory cell reaction in the submucosa and fibroblastic reaction. Control animal in series II. Hematoxylin and eosin stain;  $\times 100$ . *B*, section of colon showing acute inflammatory reaction in the serosa. Fibroblastic reaction and granulation tissue in the submucosa. Experimental animal in series II.  $\times 100$ .

definitely delayed, as at autopsy the bowel separated easily at the site of anastomosis. No gross evidence of oxidized cellulose was found.

In series II, 3 of the 4 controls survived the operative procedure. Two were killed at the end of seven days and 1 at the end of nine days. At autopsy no peritonitis was present, and the lines of anastomosis were well healed. No adhesions of the intestines to the anterior abdominal wall were found. There were a few adhesions of the omentum, ileum and colon; no abscess formation was seen. The fourth animal died at the end of twenty-four hours; it did not regain consciousness after the operation. At autopsy there was no evidence of peritonitis, the peritoneum being clean and shiny. No free fluid was found in the peritoneal cavity. No leakage from the line of anastomosis was present.

Histologically, the serosa in these animals was clean; there was a small amount of hemorrhage, with a few chronic inflammatory cells near the point of suture. Granulation tissue with some acute and chronic inflammatory cells was seen. The serosa showed slight thickening. The line of suture was closed by young fibrous tissue with ingrowth of capillary vessels. Mitotic figures were seen in the fibroblastic tissue. Figure 3A is a photomicrograph illustrating the changes described in this paragraph.

The histologic examination in the animal dying in twenty-four hours showed acute and inflammatory cells in the wall of the bowel. No granulation tissue was present. The serosa of the bowel was clean.

Four animals were used in the experimental group, these animals having the suture line protected by an eight-ply layer of oxidized cellulose. All 4 survived the operative procedure. They were killed on the fifth, sixth, eighth and eleventh day postoperatively. At autopsy none of these animals showed generalized peritonitis. All of them had many firm, dense adhesions between the omentum, the ileum and the colon. In the middle of the mass of adhesions in all the animals was found an abscess filled with purulent material. No evidence of oxidized cellulose was found in any of them.

Histologically, a thick layer of purulent exudate was seen on the serosal layer of the colon, infiltrated with many acute inflammatory cells. In the deeper layers were capillary vessels and young fibroblasts showing mitotic figures. Occasional small abscesses were found in the submucosal layer of the bowel. Muscle was being replaced by fibrous tissue. A few giant cells were seen in the wall of the bowel. A few clumps of bacteria were seen in the exudate on the serosal layer of the bowel. Figure 3B is a photomicrograph showing the changes described here.

Tables 1 and 2 summarize the findings in the individual animals of both series.

TABLE 1.—*Results in Series I*

		Control Animals
Died.		Results
24 hr.		Acute generalized peritonitis; gangrene of colon; free fluid in abdomen; ileus; no healing of anastomosis
48 hr.		Acute peritonitis; free fluid in abdomen; ileus; gangrene of colon; no healing of anastomosis
96 hr. (killed)		No healing of anastomosis; many adhesions between omentum, ileum and colon; localized peritonitis
		Experimental Animals (Oxidized Cellulose)
24 hr.		Purulent peritonitis, free fluid in abdomen and exudate on bowel; ileus; no healing of anastomosis, with leakage from suture site; 1 small piece of oxidized cellulose
24 hr.		Purulent peritonitis, free fluid in abdomen and no healing of anastomosis, with leakage from suture line; no evidence of oxidized cellulose
24 hr.		Same as in dog no. 2
48 hr.		Acute purulent peritonitis; free fluid and exudate in peritoneum; ileus; no evidence of healing of anastomosis, with leakage from the line of anastomosis; no evidence of oxidized cellulose
5 days		Eviscerated; many adhesions between omentum, ileum and colon; no definite healing of anastomosis, localized peritonitis; no evidence of oxidized cellulose

TABLE 2.—*Results in Series II*

		Control Animals
Dog	Survival	Result.
1	24 hr.	No peritonitis; no free fluid in abdomen; serosa smooth and shiny, no exudate no leakage from anastomotic site; death probably due to anesthetic
2	6 days (killed)	No peritonitis; no adhesions to anterior abdominal wall; adhesions between omentum, ileum and colon; no abscess cavity; anastomosis well healed
3	6 days (killed)	No peritonitis; anastomosis well healed; omentum attached to lateral side of colon; no adhesions between ileum and colon; no abscess
4	9 days (killed)	No peritonitis; few omental adhesions; colon anastomosis secure and well healed; no adhesions between ileum and colon; no abscess formation
		Experimental Animals (Oxidized Cellulose)
1	5 days (killed)	No generalized peritonitis; many adhesions between omentum, ileum and colon; no evidence of oxidized cellulose; abscess in middle of mass of adhesions
2	6 days (killed)	No generalized peritonitis; adhesions between omentum, ileum and colon; no evidence of oxidized cellulose; abscess cavity in middle of mass of adhesions
3	8 days (killed)	No generalized peritonitis; adhesions between omentum, ileum and colon; no evidence of oxidized cellulose; abscess cavity in middle of mass of adhesions
4	11 days (killed)	No generalized peritonitis; adhesions between omentum, ileum and colon; no evidence of oxidized cellulose; abscess cavity in middle of mass of adhesions

## COMMENT

The animals of series I were admittedly subjected to an extreme experiment to determine if oxidized cellulose would seal the suture line till healing or at least agglutination of the anastomosed ends of the bowel had taken place. Since Burns<sup>9</sup> found that oxidized cellulose early formed a gelatinous mass, the hope was entertained that this material might serve as an agglutinating factor to seal the ends of the bowel and thus prevent leakage of the intestinal contents. This hope was not realized, since 4 of the 5 animals of the experimental group did not survive the operation for a longer period than did the controls. It was further found that oxidized cellulose grossly disappeared much more rapidly from the infected peritoneal cavity than in the animals of Burns's<sup>9</sup> uninfected group. This disappearance may be due to the fluid concentration and the changes in hydrogen ion concentration reported to be present in the early phases of the infection. The disappearance of so large an amount of foreign material in so short a time apparently is not due to the action of the phagocytes. However, the cause of the rapid disappearance was not investigated at this time. It was further observed in microscopic sections that bits of oxidized cellulose appeared to induce a greater tissue reaction of inflammatory cells than occurred in the controls. Furthermore, clumps of bacteria were noted about and within the particles of oxidized cellulose; the latter may well serve as a nidus for the growth of pathogenic intestinal bacteria.

No conclusions can be drawn from the fact that 1 animal of the control group and 1 in the experimental group in series I did not succumb as early as did the other animals of this series. The matter of individual resistance to the spread of peritonitis plays a factor in either death or survival. It seems that such a factor protected these animals, since they were subjected to the same procedure as were the other animals.

In series II the experimental animals presented many more intra-peritoneal adhesions than did the controls, which confirmed Dmytryk's<sup>10</sup> observation that oxidized cellulose will not prevent adhesions. In fact, from the results in these animals one may conclude that formation of adhesions is enhanced by the presence of this material. From the observations in the first series one can conclude that the additional inflammatory reaction induced by the oxidized cellulose will result in increased adhesions in the peritoneal cavity.

The finding of an abscess within the mass of adhesions in all the experimental animals of series II in which oxidized cellulose had been used was entirely unexpected. The explanation of this happening seems to be the fact that oxidized cellulose was placed in a potentially

infected field. Conditions favorable to bacterial growth such as warmth, fluid concentration and the presence of a soluble form of cellulose were met for the formation of an abscess. This theory is shown more plausible from observations in the first series, in which microscopic examination showed many clumps of bacteria in and about the particles of oxidized cellulose remaining on the serosa of the bowel.

#### SUMMARY AND CONCLUSIONS

1. Oxidized cellulose did not prevent leakage from the anastomotic line in dogs when a single through-and-through suture end to end anastomosis was performed.

2. In the presence of infection in the peritoneal cavity of dogs, oxidized cellulose disappeared more rapidly.

3. Particles of oxidized cellulose appeared to promote the growth of bacteria in the infected peritoneal cavity of dogs.

4. In the presence of infection, oxidized cellulose appeared to induce increased formation of fibrous adhesions.

5. Abscess formation within the mass of adhesions formed when oxidized cellulose was placed in the potentially infected peritoneal cavity occurred in all the experimental animals used in series II.

6. In the presence of a potential infection in an operative field within the peritoneal cavity, the use of oxidized cellulose seems to be hazardous.

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#### CORRECTION

In the article entitled "Lymphosarcoma of the Duodenum: Report of a Case; Review of the Literature," by Dr. Murray M. Copeland and Dr. D. James Greiner, which was published in the April 1949 issue of the ARCHIVES, the sidehead "Histopathologic Fracture" on page 524, line 8, should read "Histopathologic Features."

## INCREASE OF SERUM LIPASE IN EXPERIMENTALLY INDUCED APPENDICAL PERITONITIS

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THE USE of determinations of serum amylase and serum lipase in the diagnosis of diseases involving the pancreas has achieved great prominence during the past ten years.<sup>1</sup> Increases of serum amylase have been reported in cases of acute pancreatitis,<sup>2</sup> perforation of peptic ulcer into or near the pancreas<sup>3</sup> and trauma to the pancreas.<sup>4</sup> High

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transient increases have been obtained experimentally in cases of complete obstruction of the pancreatic ducts,<sup>5</sup> and a continued increase for over a year following permanent closure of the ducts has been reported.<sup>6</sup> Hyperamylasemia has also been observed in diseases of the salivary glands such as mumps,<sup>7</sup> although here also some investigators have ascribed the increase to transient pancreatitis.<sup>8</sup> The mass of evidence at hand,<sup>7b,c</sup> however, would indicate that the high amylase level in cases of mumps occurs most frequently without evidence of involvement of the pancreas.

The appearance of hyperamylasemia is explained on the basis of retrograde passage of the enzyme into the blood and lymph either through mechanical obstruction of the pancreatic duct (or parotid duct in cases of mumps<sup>9</sup>) or through the liberation of the enzyme as a result of acute damage or destruction of the parenchymatous cells which form the enzyme.<sup>8a</sup>

Decreased values for serum amylase have been obtained in cases of increased thyroid activity<sup>10</sup> and of impaired hepatic function.<sup>11</sup> It is felt<sup>10a</sup> that the decrease found in hyperthyroidism reflects an impairment of hepatic function. Decreased values have also been reported in distur-

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bances of carbohydrate metabolism,<sup>10b</sup> although Sorkin<sup>2g</sup> noted no change in 56 cases of diabetes mellitus.

Increases of serum lipase are felt to be a more accurate index of the involvement of the pancreas in disease.<sup>1</sup> Hyperlipasemia has been reported in cases of acute pancreatitis,<sup>12</sup> carcinoma of the pancreas,<sup>13</sup> cholelithiasis with jaundice,<sup>14</sup> and chronic pancreatitis.<sup>15</sup> Increased values have also been observed in cases of peptic ulcer perforating into the pancreas<sup>2b</sup> and in cases of pancreatic cyst.<sup>16</sup> They have been obtained experimentally after trauma to the pancreas or obstruction of the major pancreatic ducts.<sup>17</sup> Although high serum lipase levels have been reported in certain conditions in which involvement of the pancreas cannot be definitely incriminated, such as mumps,<sup>7b</sup> severe destruction of hepatic parenchyma<sup>12b</sup> and intestinal obstruction,<sup>18</sup> Johnson and Bockus<sup>12c</sup> have emphasized the specificity of the serum lipase levels in diseases involving the pancreas and have stressed the value of serial determinations.

During the course of some experiments on the role of the pancreatic enzymes in intestinal obstruction, we became interested in alterations of the serum lipase in cases of peritonitis, and we were stimulated to study the serum lipase in dogs with induced severe appendical peritonitis. The hyperlipasemia was detected by means of serial determinations.

Serial determinations of serum amylase were also made, and while no significant concomitant increase of amylase occurred, interesting findings developed which would add further evidence of the hepatic origin of this enzyme, and these findings will be the basis for a subsequent report.

#### MATERIAL AND METHODS

The saccharogenic method for determining serum amylase, as outlined by Somogyi<sup>19</sup> and recommended as being the most accurate of the

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14. Comfort and Osterberg.<sup>2b</sup> Johnson and Bockus.<sup>12b</sup>

15. Comfort and Osterberg.<sup>2b</sup> Johnson and Bockus.<sup>12c</sup>

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available methods by Dozzi,<sup>20</sup> was employed in this study. Dog serum has twenty to twenty-five times the amylase activity of human serum,<sup>21</sup> which necessitated the use of smaller amounts of serum. The presence of amylase was detected with the use of cornstarch as the substrate. One cubic centimeter of serum was added to 5.0 cc. of a 1.5 per cent starch solution plus 2.0 cc. of sodium chloride buffer and incubated at 37 C. for thirty-five minutes. Reducing sugar formed from the starch digestion was determined by the colorimetric method of Folin and Wu<sup>22</sup> using 0.1 or 0.2 cc. of the filtrate for the determination. The amount of amylase in the blood is expressed in terms of milligrams of dextrose formed from the hydrolysis of starch solution by 100 cc. of serum.

The Lovenhart modification of the method of Cherry and Crandel<sup>17</sup> was used for the determinations of serum lipase. The amount of lipase in the blood is expressed in terms of cubic centimeters of 0.05 normal sodium hydroxide required to neutralize the fatty acids liberated by the action of 1.0 cc. of serum on an olive oil emulsion.<sup>23</sup> In the majority of cases determinations were run in duplicate. We have done over four hundred determinations of lipase in serum, duodenal contents and pure pancreatic juice and have been impressed with the consistency of the results. In a number of the animals operated on the specific gravity of the blood and plasma,<sup>24</sup> blood urea nitrogen<sup>25</sup> and blood chlorides<sup>26</sup> were determined.

Both normal animals and those operated on were placed on a standard diet of water and purina<sup>®</sup> dog biscuits for twelve to twenty-four hours before the blood samples were taken, and the dogs which were operated on were starved for twenty-four hours before operation. The blood samples were rapidly withdrawn from the femoral artery into a dry, sterile syringe, and the serum was immediately removed after the sample was centrifuged at 2,500 revolutions per minute for fifteen minutes.

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Every effort was made to obviate hemolysis as a source of error in the determinations. The samples were taken usually between 8 and 11 o'clock in the morning and were immediately analyzed. Eighty determinations of serum amylase and ninety-two determinations of serum lipase have been made on 46 and 51 normal dogs, respectively, prepared in this fashion.

In the experiments on animals with peritonitis 14 mongrel adult dogs weighing between 7.0 and 13.0 Kg. were used. Control determinations were taken the day before and the morning of operation. During the operations pentobarbital sodium (24.0 mg. per kilogram) was employed, and aseptic technic was used throughout. The abdomen was opened through a low right rectus incision and closed in three layers with silk. Peritonitis was induced in one of two ways. In 11 of the animals, subsequently referred to as group I, fulminating peritonitis was created by ligating and slitting the appendix after the method of Zintel, Wiley, Nichols and Rhoads.<sup>27</sup> as recommended by Harvey, Meleney and Rennie.<sup>28</sup> In 3 of the animals, subsequently referred to as group II, peritonitis was created by ligation of the appendix alone after the method of Fauley and his group<sup>29</sup> and Kay and Lockwood,<sup>30</sup> modified in that all the omentum distal to the spleen was removed at operation. Five of the 14 animals survived for ten days or longer (dogs 71, 69 and 1385 in group I and dogs 125 and 1398 in group II). This report is primarily concerned with these 5 animals. The remaining 8 dogs in group I all died of fulminating peritonitis between twelve and thirty-two hours after operation, with an average survival time of twenty hours. The remaining animal in group II also died of fulminating peritonitis between ninety-six and one hundred and four hours after operation. In addition to the water and dog biscuits allowed postoperatively, 4 of the 5 surviving animals received isotonic sodium chloride solution intravenously (40.0 to 100 cc. per kilogram every twenty-four hours) and penicillin-in-oil (150,000 units every twelve hours) for the first twenty-four to forty-eight hours, at which time these extra measures were discontinued. Dog 69, the fifth animal, received no treatment other than the standard diet. Generalized peritonitis was manifested in

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27. Zintel, H. A.; Wiley, M.; Nichols, A., and Rhoads, J. E.: The Use of Streptomycin in Surgical Patients, *Surgery* **21**:175, 1947.

28. Harvey, H. D.; Meleney, F. L., and Rennie, J. W. R.: Peritonitis: III. Studies in Peritoneal Protection with Particular Reference to Action of Sulfonamides in Experimental Peritonitis, *Surgery* **11**:244, 1942.

29. Fauley, G. B.; Duggan, T. L.; Stormont, R. T., and Pfeiffer, C. C.: The Use of Penicillin in the Treatment of Peritonitis, *J. A. M. A.* **126**:1132 (Dec. 30) 1944.

30. Kay, J. H., and Lockwood, J. S.: Experimental Appendical Peritonitis, *Surgery* **20**:56, 1946.

all cases by the clinical course (abdominal rigidity, increase in temperature and pulse, vomiting and shock of varying degree), by the aspiration of abundant bloody peritoneal fluid, by the development of a wound abscess and by postmortem examination (in 3 of the animals killed at varying intervals). With few exceptions blood samples were taken at twenty-four hour intervals, usually between 8 and 11 o'clock in the morning, and immediately analyzed. In some cases twelve hour samples were taken in addition to the twenty-four hour specimens. When twelve hour samples were withdrawn at night, the serum was removed and immediately placed in the icebox at 0 C. to be run early the following morning. We found little, if any, diminution of the enzymatic activity

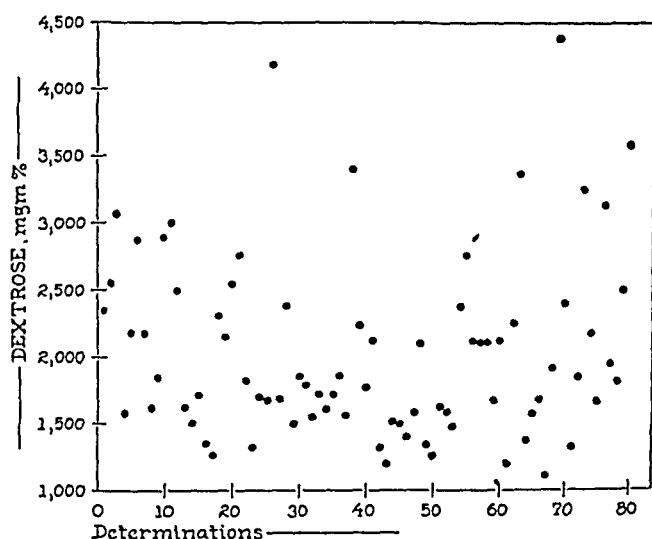


Fig. 1.—Results of eighty determinations of serum amylase on 46 normal dogs. The extreme range of variation is from 1,104 to 4,371 mg. per hundred cubic centimeters, with an average of 2,040 mg. Ninety-five per cent are in the range of 1,100 to 3,500 mg.

by this method provided the serum did not stand for longer than eight to twelve hours.<sup>5</sup>

#### RESULTS AND COMMENT

The results of eighty determinations of serum amylase on 46 normal dogs are shown in figure 1. The values ranged from 1,104 to 4,371 mg. per hundred cubic centimeters, with an average of 2,040 mg. Seventy-seven (95.5 per cent) were in the range of 1,100 to 3,500 mg. While this great variation was evident among the different animals, it was not so marked when daily determinations were done on the same animal (fig. 2). It was noted, however, that rather pronounced variations within the normal range occurred in the same animal if blood samples were taken at various periods of the day despite the fact that the dog

was always on the standard diet. Friedman and Thompson<sup>31</sup> have noted also striking spontaneous increases of serum amylase in normal dogs.

The results of ninety-two determinations of serum lipase on 51 normal dogs are shown in figure 3. Serum lipase values in the normal dog are known to be low,<sup>32</sup> and this is borne out in our studies. In only three determinations were the values 1.0 cc. or over, and two of these (2.12 and 2.50 cc.) were in the same animal on successive days. In 95 per cent of the determinations the values were below 0.7 cc. The average for all the determinations was 0.29 cc. Daily determinations for six to ten day periods in 3 normal dogs showed a great constancy of the results, and only infrequently were values of 0.6 cc. or over noted. Sodium pentobarbital anesthetic alone, when administered to normal dogs prepared in an identical manner, had no effect on the serum lipase. Not even in dogs in which we have ligated both pancreatic ducts have we noted values as high as those which Dozzi<sup>33</sup> has reported

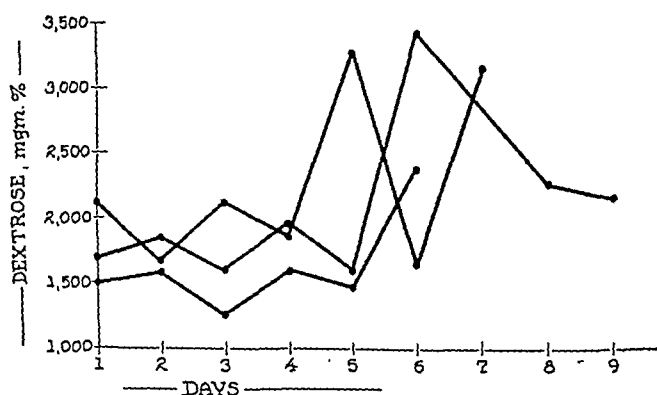


Fig. 2.—Serial determinations of serum amylase on 3 normal animals.

in 1 of his normal dogs (no. 411). We feel that values over 1.0 cc. represent a definite increase in the dog.

The results of daily determinations of serum lipase in the 5 dogs surviving fulminating peritonitis are shown in figure 4. Increases of over 1.0 cc. occurred in 4 of the 5 animals. It will be noted that the maximum increases occurred between the fourth and fifth days in the group I dogs and between the sixth and eighth days in the group II dogs. This will be referred to subsequently. It is possible that an increase above 1.0 cc. was missed in the remaining dog (no. 1385). This was

31. Friedman, I., and Thompson, W. R.: Induced and Spontaneous Changes in Blood Amylase, Particularly in Relation to Pancreas: An Experimental Study, *Ann. Surg.* **104**:388, 1936.

32. Baxter, Baxter and McIntosh,<sup>12a</sup> Cherry and Crandel.<sup>17</sup>

33. Dozzi, D. L.: Origin of Blood Amylase and Blood Lipase in the Dog, *Arch. Int. Med.* **68**:232 (Aug.) 1941.

one of the earlier dogs operated on in the series, and no samples were taken between the fourth and sixth days or after six days. On the basis of the occurrence in the other 2 dogs in this group, a rise might have been expected during the fourth to sixth days.

In view of the variations in serum amylase in serial determinations on normal dogs, we do not feel that any significance can be attached to the occasional slight and inconsistent rises noted in the surviving animals in which amylase levels were followed (fig. 5). However, the distinct and consistent decrease in the serum amylase within the first twelve to thirty-six hours after anesthesia and operation in all the animals has, we feel, considerable significance and has formed the basis for a subsequent report in preparation.

As Johnson and Bockus<sup>12c</sup> have stated, there are several explanations to account for increased lipase. Any mechanism which blocks one or more of the larger pancreatic ducts may cause an increase in the concen-

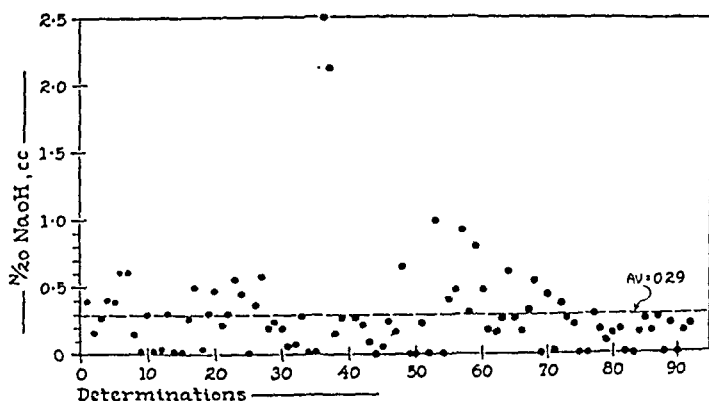


Fig. 3.—Results of ninety-two determinations of serum lipase in 51 normal dogs. Ninety-five and five-tenths per cent show levels below 0.7 cc., and in only three is the level 1.0 cc. or over. The average for all determinations is 0.29 cc.

tration of the serum lipase because of absorption of that ferment into the blood stream. Hyperlipasemia occurring in experimental ligation of one or more of the major pancreatic ducts, pressure of a tumor arising in or near the pancreas or edema of the pancreas or surrounding structures secondary to inflammatory changes would indicate this obstructive origin. A second method has been described as being the absorption of pancreatic debris secondary to an acute necrosis of the pancreas.

We feel that obstruction of the smaller ducts on the basis of an inflammatory edema is the method of production of the high lipase levels in the animals herein reported on. This has been indicated both by the serial lipase curves in the two groups of animals and by postmortem examination of the pancreas in 3 of the animals which were killed. It should be emphasized that every effort was made not to touch the

pancreas at the time of operation. We feel that trauma was not the mechanism of increase in any of these cases because after manipulative trauma to the pancreas the serum lipase rises in the first twenty-four to forty-eight hours.<sup>34</sup>

As noted (fig. 4), the maximum increase occurred after between four and five days in the animals in which the appendix had been

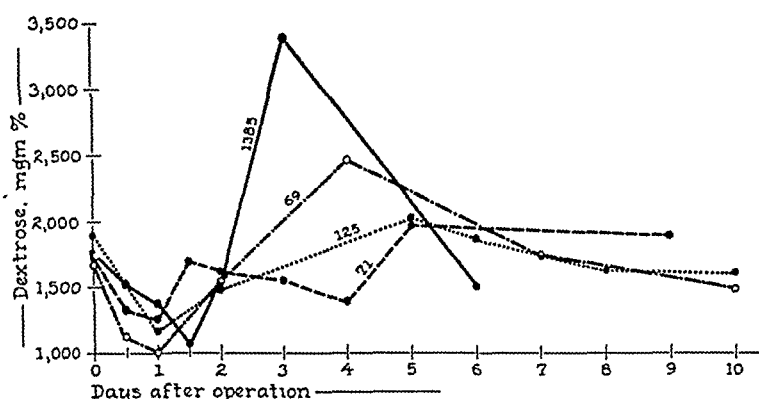


Fig. 4.—Results of serial determinations of serum lipase in 5 dogs surviving an induced, severe, fulminating appendical peritonitis for ten days or longer.

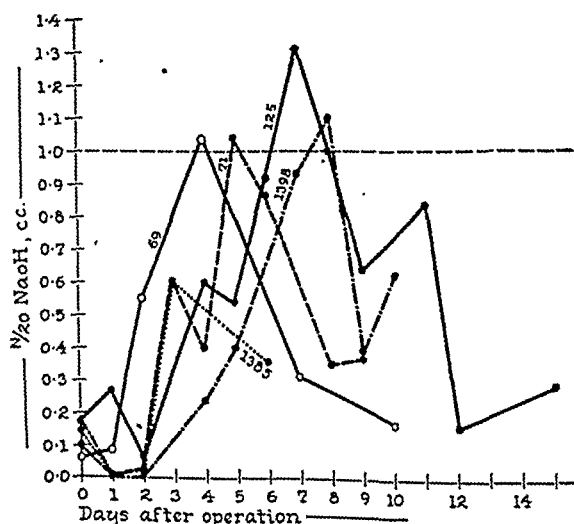


Fig. 5.—Results of serial determinations of serum amylase in 4 of the 5 animals surviving an induced, severe, fulminating appendical peritonitis for ten days or longer.

slit at operation. The onset of severe peritonitis was, therefore, immediate in this group. On the other hand, the maximum increases occurred in 6 to 8 days in the dogs in group II. Kay and Lockwood<sup>30</sup> have given a detailed analysis of the course of the animals operated on in

34. McCaughan.<sup>4a</sup> Nemir, Hawthorne and Locrone.<sup>4d</sup> Cherry and Crandel.<sup>17</sup>

this fashion and have stated that the appendix has usually not ruptured by the second day. Therefore, in this group it is likely that the onset of diffuse peritonitis does not occur until some time between twenty-four and forty-eight hours after operation. If these conclusions be valid, then the length of time of the existence of diffuse peritonitis in relation to the time of maximum increase of the serum lipase becomes uniform in the two groups. This would indicate that, in the dog at least, it takes four to five days after the onset of severe, diffuse appendical peritonitis for the pancreatic function to be sufficiently impaired to result in hyperlipasemia.

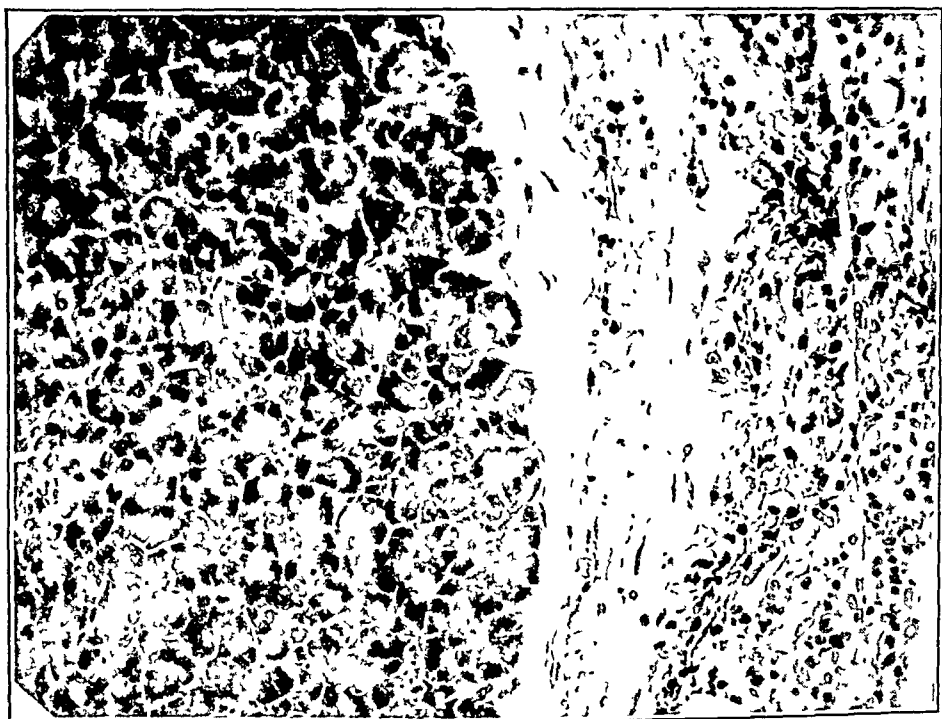


FIG. 6—Section of right limb of pancreas of dog 125 showing peripancreatic inflammation;  $\times$  221.

Further positive evidence of the mechanism of production of the hyperlipasemia was afforded by postmortem examination. Two of the dogs (no. 69 and no. 1398) were killed at ten days and 1 (no. 125) at fifteen days after operation. The findings were similar in all 3 cases. Grossly, no changes were noted other than a dulness and thickening of the peritoneum overlying the pancreas. Examinations of sections from various portions of the gland showed similar changes in all. There was severe peripancreatitis with notable edema and infiltration of cells (fig. 6). Although polymorphonuclear leukocytes were present in abundance, the predominant cells were lymphocytes and

large mononuclear cells. This peripancreatic inflammation varied in severity in the different sections from the same gland, the right limb and body being affected much more than the left limb. In general, the cells of the gland were intact, but in dog 125 there was definite intralobular edema, and in dogs 69 and 1398 there was both interlobular and intralobular edema.

Examinations of the sections of pancreas from 3 of the animals dying between twelve and thirty-two hours after operation revealed uniformly a moderate interlobular and intralobular edema, but the peripancreatitis was minimal or absent entirely, the changes being directly related to the time of survival of the animal.

A recapitulation of the course of events would therefore seem to be as follows: Within twenty-four to thirty-six hours after the onset of diffuse appendical peritonitis, the pancreas became moderately edematous, but there was no active cellular infiltration around the capsule. By ninety to one hundred and twenty hours the generalized inflammatory reaction reached its maximum, and thickening, edema and infiltration about the pancreatic capsule had occurred. We feel that it is during this time that the pathologic processes combine to cause a blockage of the smaller pancreatic ducts, with a concomitant increase of the serum lipase. Subsidence of the inflammation then occurs; the lipase rapidly returns to normal, and chronic inflammatory cells come into prominence.

#### SUMMARY AND CONCLUSIONS

1. Alterations in serum amylase and lipase in dogs having an experimentally induced severe, diffuse appendical peritonitis have been studied by means of serial determinations.

2. Of 14 animals operated on, 5 lived for ten days or longer, and 4 of these 5 demonstrated significant increases of the serum lipase. No significant concomitant increase of the serum amylase was noted in this series.

3. The maximum increase of serum lipase occurred in between four and six days after the onset of diffuse peritonitis, and the level rapidly returned to normal after the subsidence of the inflammatory reaction.

4. We feel that the mechanism of production of the hyperlipasemia is on the basis of peripancreatic inflammation and interlobular and intralobular edema, with resulting blockage of the smaller pancreatic ducts.

Dr. E. A. Case, of the Graduate School of Medicine, interpreted the histologic sections.



## SARCOMA OF THE ESOPHAGUS

Report of Successful Resection of a Fibrosarcoma

DWIGHT EDWIN CLARK, M.D.

CHICAGO

**P**RIMARY sarcoma of the esophagus is a rare condition. Dvorak<sup>1</sup> in 1931 presented an excellent discussion of the entire subject and reviewed the reported cases up to that time. He found less than 50 cases in the literature, and in many of these there was considerable doubt concerning the exact pathologic process. Simon<sup>2</sup> three years earlier was able to collect only about 30 unquestioned cases.

Since 1931 there have been few additional cases of primary sarcoma of the esophagus reported. Jaleski and Waldo<sup>3</sup> described an interesting case of a primary melanotic sarcoma of the esophagus which was not diagnosed before autopsy. The tumor was polypoid, and there was extensive metastasis to the lungs, liver, pancreas, spine and regional lymph nodes. Cases of primary leiomyosarcoma of the esophagus have been contributed by Mallory,<sup>4</sup> Menne and Birge,<sup>5</sup> French and Garland<sup>6</sup> and Pennes.<sup>7</sup> Bayer<sup>8</sup> in 1941 reported on a patient with sarcoma of the esophagus free of symptoms fifteen months after roentgen ray therapy. The following case is presented because of the rarity of the condition and because no known successful resection of a primary sarcoma of the esophagus has been reported.

C. P., a white man aged 43, was admitted to the Oak Ridge Hospital on Feb. 22, 1947. About eight months before he had first noticed some difficulty in swallowing

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From the Department of Surgery, University of Chicago.

1. Dvorak, H. J.: Sarcoma of the Esophagus, *Arch. Surg.* **22**:794 (May) 1931.

2. Simon, H.: Die Sarcome, *Neue deutsche Chir.* **43**:246, 1928.

3. Jaleski, T. C., and Waldo, P. V.: Primary Melanotic Sarcoma of the Esophagus, *Am. J. Cancer* **24**:340, 1935.

4. Leiomyosarcoma of Distal Third of Esophagus with Extension into and Ulceration of Mediastinal Lymph Nodes, Cabot Case 21501, *New England J. Med.* **213**:1194, 1935.

5. Menne, F. R., and Birge, R. F.: Primary Leiomyosarcoma of Upper Third of Esophagus, *Am. J. Digest. Dis.* **3**:848, 1937.

6. French, L. R., and Garland, L. H.: Leiomyosarcoma of the Esophagus, *Am. J. Roentgenol.* **45**:27, 1941.

7. Pennes, A. E.: Leiomyosarcoma of the Esophagus, *Am. J. Roentgenol.* **48**:336, 1942.

8. Bayer, L.: Ueber ein mit Röntgenstrahlen beseitigtes, seit 15 Monaten symptomfreies Sarkom de Speiseröhre, *Monatschr. f. Krebsbekämpf.* **9**:86, 1941.

solid foods. This dysphagia lasted about one month and then suddenly disappeared. For the next six months he was able to eat all kinds of food without any discomfort. One month before his admission he again began to have dysphagia, which rapidly progressed until he had difficulty even swallowing liquids. He became extremely weak and lost 30 pounds (13.6 Kg.) of weight. He never had a cough, but for several days prior to his admission his voice had been hoarse. The past history was noncontributory.

*Physical Examination.*—The patient appeared chronically ill, with obvious signs of recent loss of weight. There was no dyspnea. A definite hoarseness was noted. The lungs were clear. The heart rhythm was regular, and no murmurs could be heard. The blood pressure was 140 systolic and 90 diastolic and the pulse rate 70. The reflexes were equal and active.



Fig. 1.—Roentgenograms of esophagus after ingestion of barium. Anterior and lateral views show a large filling defect in the upper region extending from the level of the clavicles to below the arch of the aorta. The esophagus in the region of the tumor has dilated, allowing barium to flow around the mass.

*Laboratory Data.*—All blood counts were within normal limits. The urine was normal, and the Wassermann reaction was strongly positive. Roentgenologic examination after the administration of barium revealed a large polypoid mass in the upper part of the esophagus which filled the entire lumen (fig. 1). The pulmonary fields were normal.

*Esophagoscopy.*—At 26 cm. from the upper incisors an irregular grayish brown firm mass was seen which filled the entire lumen of the esophagus. There was definite dilatation of the esophagus above the tumor. A biopsy was performed, which showed the lesion to be a fibrosarcoma.

*Preoperative Preparation.*—The patient received a high protein liquid diet supplemented with vitamins. In addition he was given one blood transfusion and

500 cc. of plasma. Large doses of penicillin were given in order to render the patient noninfective from a syphilitic standpoint.

*Operation.*—Cyclopropane, ether and oxygen anesthesia administered through an endotracheal tube was employed. The patient was placed on his right side and the left side of the chest opened through the bed of the sixth rib, which had been removed subperiosteally. The third, fourth, fifth and seventh ribs were transected posteriorly near their accompanying transverse processes and the intercostal structures between these ribs divided and ligated. A 2 cm. segment of the left phrenic nerve was excised in order to paralyze permanently



Fig. 2.—Roentgenogram of esophagus and stomach following ingestion of barium, fourteen days after resection and esophagogastrostomy. It shows all of the stomach in the thorax. The anastomosis is above the level of the clavicle, and the diaphragm is closed around the pylorus.

the left leaf of the diaphragm. Exploration of the mediastinum failed to reveal any evidence of metastasis. The esophagus was freed from the posterior mediastinum from just above the esophageal hiatus upward to the arch of the aorta. The vagus nerves were sacrificed. The lower portion of the tumor mass was located just below the arch of the aorta, and in order to facilitate mobilization of the esophagus in this region the mediastinal pleura was incised above the arch of the aorta and lateral to the left subclavian artery. By means of blunt dissection both above and below the arch of the aorta, the esophagus was readily freed from the adjacent mediastinal structure. A small firm node attached to the carina was removed.

The upper portion of the tumor extended into the base of the neck and necessitated freeing of the esophagus above the level of the sternal notch. The abdomen was now entered through a radial incision in the left side of the diaphragm. There was no gross evidence of metastasis. The spleen was removed. The upper four fifths of the stomach was mobilized by dividing the omentum distal to the gastroepiploic vessels and the left gastric artery close to its origin from the celiac axis. The stomach was transected just below the cardioesophageal junction and the

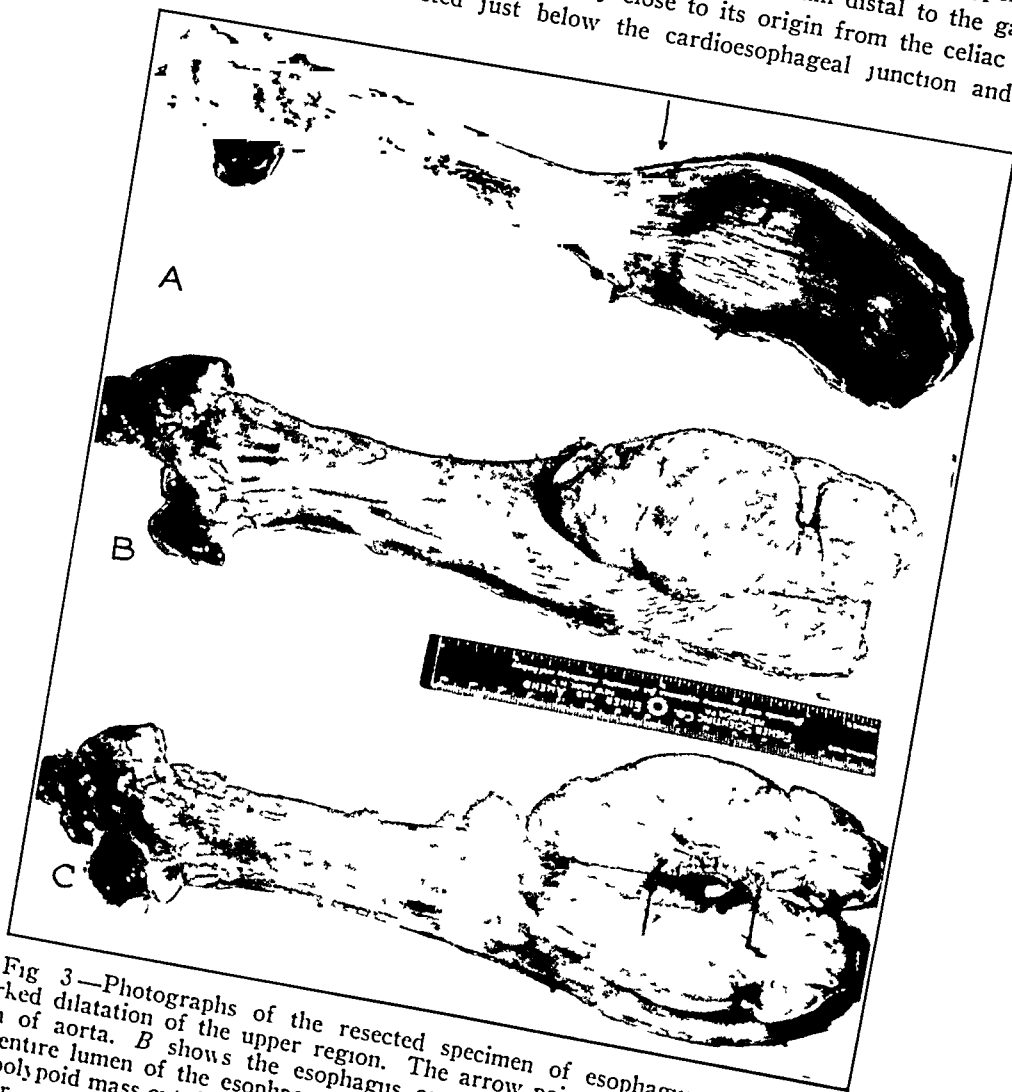


Fig 3—Photographs of the resected specimen of esophagus. *A* shows the marked dilatation of the upper region. The arrow points to depression caused by arch of aorta. *B* shows the esophagus open. Note large polypoid mass filling the entire lumen of the esophagus. Gastroesophageal junction is shown. *C* shows the polypoid mass cut through the center. Area between arrows shows pedicle of the tumor.

The mobilized esophagus was drawn out through the distal opening infolded. The opening in the mediastinal pleura above and to the left of the arch of the aorta was easily brought up to the base of the neck and an anastomosis made between the esophagus and an opening in the fundus of the stomach. The esophagus was transected 4 cm above the upper limit of the tumor. In spite of the high position of the anastomosis there was no apparent tension on the suture

line. The diaphragm was closed about the pylorus, and the chest was closed tightly. A catheter was brought out through the ninth inner space for pleural drainage. The patient received 2,500 cc. of blood during the operation.

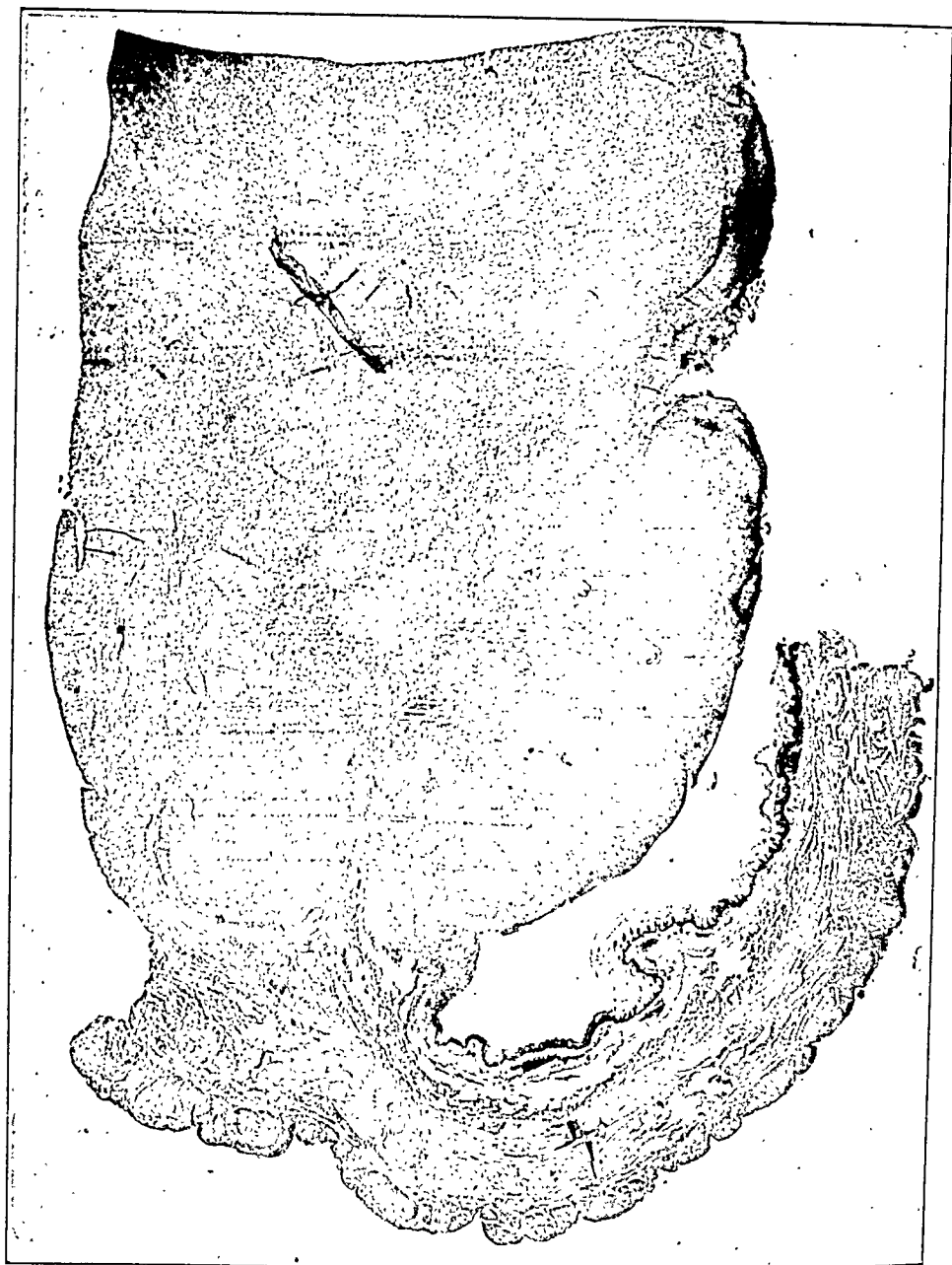


Fig. 4.—Photomicrograph in region of the pedicle of the tumor. The tumor is shown to be well circumscribed and is arising from the submucosa. There is no invasion into the muscularis.

*Postoperative Course.*—The patient had an uneventful convalescence. A stomach tube which had been placed at the time of operation was connected to a suction apparatus and negative pressure maintained for seventy-two hours. From the

third to the ninth day he was given small amounts of nourishing liquids every hour through this tube. On the ninth day the tube was removed and he was started on oral feedings, which he tolerated well. Antibiotics were given for ten days. Blood and plasma were administered as needed. He was up and walking about the ward on the seventh day and was discharged on the fourteenth post-operative day. Roentgenologic examination after a swallow of barium made two weeks postoperatively revealed the entire stomach in the thorax and a well functioning esophagogastrostomy opening. The site of anastomosis was above the level of the clavicles (fig. 2). He returned to work two weeks after his discharge from the hospital.

*Pathologic Report.*—Gross Examination: The specimen consisted of 28 cm. of esophagus. The upper 11 cm. was dilated and the lumen filled with a firm, elastic,

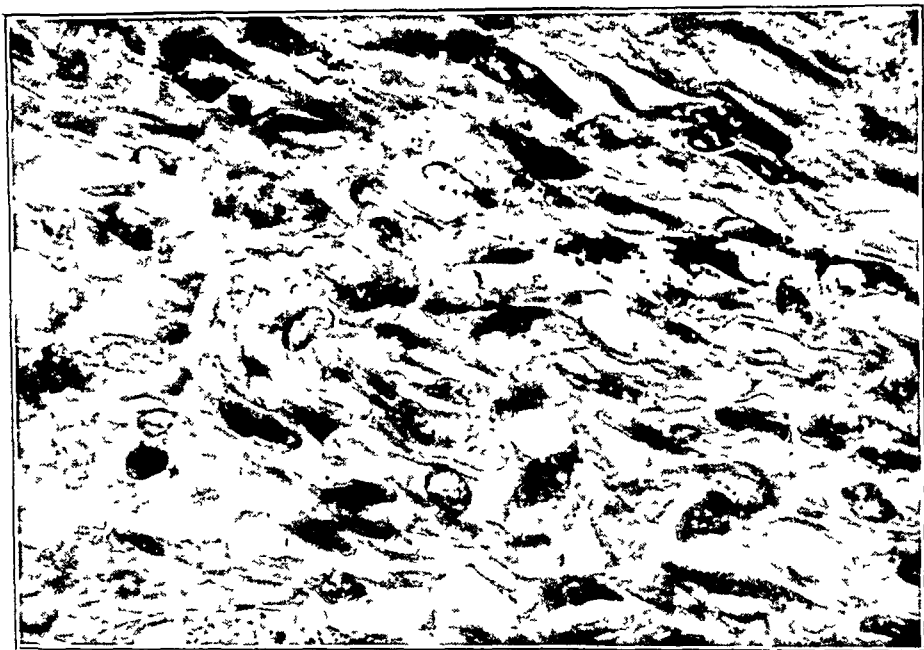


Fig. 5—Photomicrograph showing the tumor to be composed of connective tissue cells. Myofibrils could not be demonstrated by phosphotungstic acid and hematoxylin stains.

bulbous growth. The open esophagus presented no noteworthy changes except for a tumor mass which measured 12 cm. in length and 4.5 cm. in diameter. The surface of the tumor was lobulated and grayish red with scattered areas of yellow. It was attached to the posterior wall of the esophagus by a pedicle measuring 4.5 cm. by 0.4 cm. (fig. 3). The cut surface was relatively uniform and presented a slightly moist, pale appearance with a grayish red tracery. There were occasional areas of softening.

*Microscopic Examination:* The tumor seemed to arise from the submucosal region and did not invade the muscularis. The surface of the growth was devoid of epithelium (fig. 4). The mass was composed of cells presenting the configurations of connective tissue cells. These cells varied in size, shape and staining properties. Some had large nuclei; others were vesicular, with prominent nucleoli. There was considerable hyperchromasia and a moderate number of mitotic figures. Phosphotungstic acid stains did not reveal any myofibrils (fig. 5).

## COMMENT

Sarcoma of the esophagus is clinically differentiated from carcinoma with difficulty. The symptoms of the two are similar. The age distribution and sex incidence are the same as that of carcinoma.

Sarcomas of the esophagus are usually divided into two general groups, the diffuse infiltrating type and the polypoid type. The former contain round or polyhedral cells and metastasize early, while the latter are usually composed of spindle cells and metastasize late.

In the case presented there was a history of progressive difficulty in swallowing which began eight months before the patient's admission to the hospital. The dysphagia lasted for about one month and then suddenly subsided. It is probable that a polypoid growth was present at *that time which was similar to that found at the time of operation* but because of the peristaltic movements of the esophagus and the pressure exerted by the ingested food the mass broke off, relieving the obstruction. During the ensuing six months the polypoid growth slowly recurred. In spite of the long history and the large size of the intraluminal growth there was no evidence of invasion through the wall of the esophagus. The node removed from the carina showed invasion with tumor cells and was the only evidence of metastasis found.

Although there is considerable disturbance of gastrointestinal physiology associated with esophagectomy, this patient had little difficulty after the operation. He was able to eat well, had the sensation of hunger and never experienced any regurgitation of gastric contents.

Preservation of an adequate blood supply to the esophagus and stomach is of prime importance in the successful outcome of high esophageal resections. Division of the esophagus should be high enough to reach the esophageal branches of the inferior thyroid artery. Mobilization of the stomach should be carried out so as to preserve the arcade of vessels on the greater and lesser curvatures.<sup>9</sup> If these arcades are preserved to supply adequately the intercommunicating vessels within the wall itself, the stomach can be mobilized down to the pylorus without any fear of necrosis.

## SUMMARY

A fibrosarcoma of the upper part of the esophagus was successfully resected. The esophagogastric continuity was reestablished by an anastomosis between the stomach and the esophagus over and above the arch of the aorta.

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9. Clark, D. E.: Transthoracic Esophagogastrostomy for Carcinoma of the Middle Third of the Esophagus, *Ann. Surg.* **121**:65, 1945.

## NEW ADVANCES IN SEAMLESS PROSTHETIC HANDS

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AND

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IN A PREVIOUS article, "Seamless Prosthetic Hands: A Technic of Fabrication."<sup>1</sup> methods of producing prosthetic rubber and plastic hands in rubber molds were explained in detail. Since the appearance of this article, numerous advances have been made. They are primarily new methods of producing molds and improved plastics and a technic of making partial hands.

### ELEMENTARY CONSIDERATIONS

Nineteen years ago one of us (C. D. C.) produced seamless electroplated molds over actual amputated hands. Agar molds were also used to cast seamless wax hands, which were treated with graphite and electroplated. In any event, both methods produced difficulties. The actual dead hand could serve as a pattern only once. It was possible to get no more than one wax hand out of an agar mold. Suitable resilient plastics had not been discovered at that time. Therefore, rubber was the prosthetic material of choice. Even today some workers are making plastic impressions in sodium alginate composition molds. This material is similar to agar and also a derivative of kelp. It permits only one good impression in the plastic. The rubber mold as described in the previously mentioned article permits the making of fifteen good plastic hands before the mold deteriorates. In spite of this fact, the demand for prosthetic hands is so great that it has become necessary to return to the electroplated metal mold for quantity production. From a single such mold, hundreds of plastic positive prosthetic hands may be obtained.

These resilient resin casts or skinforms possess a wealth of surface detail, a lifelike luminosity with rubber-like resiliency and strength. They are also entirely devoid of the seam or join lines inevitable when

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From the Plastic Artificial Eye and Restorations Research Laboratory, Veterans Administration, School of Medicine, University of Maryland.

1. Clarke, C. D.; Weinberg, F. B., and Blevins, G. C.: Seamless Prosthetic Hands: A Technic of Fabrication, *Arch. Surg.* **54**:491-516 (May) 1947.



two piece molds are employed. They make ideal models or patterns from which metal quantity molds may be made by electroforming. Unfortunately latex molds have a short productive life, since only about fifteen casts may be made from a single mold. Nevertheless, all fifteen can serve as patterns for electroplating or electroforming. The chief limitation of the latex mold lies in the disparity in the curing temperature of rubber latex and vinyl plastic. The temperature of 130 C. required to cure most of the vinyl resins would completely destroy a latex mold, since rubber resinifies or becomes syrupy at 125 C.

In order to overcome this difficulty, we remove the mold when the cast is partially cured, or "turned over" as expressed by the trade. That is, after it has been in the oven for forty-five minutes at 100 C. and is sufficiently strong to be separated without danger of tearing. The removed cast or skinform is then immersed in a glycerin bath at 130 C. for a final cure. This method is superior to raising the temperature slowly with the cast immersed, because of the danger of overheating and blistering the cast. On cooling, the completely cured cast is removed and the glycerin washed off in running water. While the hand may be carefully removed from the hot glycerin with blunt instruments, the plastic skinform while hot is extremely friable and inadvertent handling or strain will cause it to fracture. The glycerin-cured cast will have a more lifelike appearance as well as greatly increased resistance to wear and tear. Skinforms prepared in such a manner are entirely satisfactory for making the actual hand prosthesis. However, because of the fact that only fifteen skinforms may be obtained from a single rubber mold, these are used as patterns for making metal molds capable of producing thousands of identical duplicates.

The problems of producing these electroplated molds over the plastic hands that were obtained from rubber molds were many. Most plastics are excellent electroinsulating materials. The hand must be made conductive to electricity. Graphite was applied with a brush, as is done in electrotyping. While excellent deposits could be obtained, the surface so treated would not conduct electricity. Bronze and brass lacquers were used, as is done on leather for making this material conductive to electricity. This method worked, but the thicker coats of lacquer powder mixture destroyed some of the surface detail of the plastic. It must be borne in mind that the plastic hand should have every pore detail in sharp relief. The cast must produce fingerprint patterns; otherwise the prosthesis suffers by comparison with a real hand. The bronze lacquer was discarded. It was then decided to attempt to produce a silver deposit on the pattern, as is used in silvering mirrors. Such deposits are electroconductive, and at the same time the deposit is so thin that none of the infinite details is lost.

## REPAIR OF VINYL PLASTICS

Before a plastic skinform is used for a pattern in electroplating, it must be correct in every detail. As a result of undue stress and strain while hot, the vinyl plastics are sometimes torn. If these tears are extensive, the hand is discarded. Small torn places may be repaired as follows: Particles of the cured vinyl plastic are put into a large-mouthed bottle of cyclohexanone and shaken from time to time until dissolved. This solution of cured vinyl acetate-chloride in cyclohexanone makes an excellent repair medium or cement. A small amount of this cement is brushed on the edges to be joined with a small camel hair brush. The edges are approximated and the surplus medium removed with a dry cloth. Drying should continue until the cyclohexanone is completely volatilized.

## ESSENTIAL STEPS IN THE PROCESS

The formation of suitable metal molds involves a series of definite steps which are as follows:

1. Mechanically stiffening the flexible pattern with a wax support.
2. Attaching the cathode wires.
3. Cleaning the surface.
4. "Sensitizing" the surface.
5. Formation of the silver electroconducting film by chemical reduction.
6. Electroplating the surface.
7. Metal spraying the surface for thick build-ups.
8. Removing the pattern.
9. Applying the separating medium.
10. Making the plastic duplicate.

## MECHANICALLY STIFFENING THE PATTERN

A thin pattern must be chosen for the electroplating or metal-spraying process. Otherwise extreme difficulty will be experienced in removing the pattern from the final metal mold. The plastic or rubber hand on removal from a rubber or metal mold is soft and flexible. Such a pattern is not sufficiently rigid to stand alone. To prepare a metal mold from the skinform, it becomes necessary to make the hand temporarily rigid or stiff enough to stand, without bending, the pressure of air spraying in sensitizing, silvering and the general handling necessary during the first stages of electroplating. To accomplish this we simply pour the hand full of melted waxes, while lowering it into a vessel of cold water. The internal pressure of the wax against the pressure of the water on the external surface of the hand prevents it from becoming distorted. At the same time, the cold water sets the wax in an even deposit on the inner surfaces of the hand. A deposit of

about 3 mm. of wax is allowed to build up on the inner surface, and then the excess wax is poured back into the pot.

A fifty-fifty mixture of paraffin and B square microcrystalline wax<sup>2</sup> serves excellently for this purpose. The thickness of the deposit can be determined during the build-up by simply blowing the liquid wax away from an edge. The set or congealed wax remains and is distinguishable from the liquid wax. It is best not to pour the wax into the hand until it has cooled sufficiently to be handled without burning the fingers. Furthermore, under such conditions, the build-up takes place in less time. Extreme care must be taken to prevent the wax from overflowing to the outer or skin surface of the hand. If this happens details on the surface of the hand will be lost and the silver spray and electroplated deposits will not stick. If the deposit of wax is too thick or the hand is entirely solid with wax, it will float in the electroplating bath, making the plating difficult or impossible.

After wax of proper thickness is deposited within the hand, it is ready to receive the connectors between the electrode and the hand. These are made of heavy copper wire, attached to three battery clamps. One battery clamp is connected to the center of a 6 inch (15 cm.) piece of 8 gage copper wire. One clamp is then fixed to each end of the wire. These end clamps are attached to the plastic hand. All silver-spraying and metal-plating operations are now carried out while the hand is attached to the connectors.

#### CLEANING THE SURFACE

The proper preparatory treatments of plastic surfaces are the governing factors which make for the success or failure of any process for "silvering" plastics. This "deglazing" or "degreasing" of the plastic surface, its cleaning and so-called "sensitizing" or making the surface more receptive to the conductive film to be formed thereon are important steps in the process which cannot be overlooked. Even fingerprint marks or grease marks must be washed away. Otherwise a nonadherent and mottled silver film may result.

It is a well known fact that sprayed or electroplated metal deposits do not readily stick to greasy surfaces. Plastic hands as obtained from rubber molds, while in the strictest sense not greasy, nevertheless must be treated with a degreasing agent before silver spraying. The areas between the fingers seem to be particularly susceptible to this non-sticking of the silver deposit, which invariably results in a failure of a uniform electrodeposit of metal. We found that the hands could be cleaned by scrubbing with a wet brush dipped in plaster of paris or better still washed with one of the detergents such as a fairly concen-

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2. Bereco Oil Company, Tulsa, Okla

trated solution of trisodium phosphate. These hands could be degreased with carbon tetrachloride. The latter method, while satisfactory, was more costly and troublesome. We finally used the trisodium phosphate for the degreasing process. The hands were simply dipped into the semiconcentrated solution and the surface scrubbed with a brush. Or they can be soaked in the solution for half an hour. The plastic pattern should be thoroughly rinsed in water to remove the cleaning agent. The next step in the process is carried out while the hand is still wet.

It is then necessary to sensitize the plastic to receive the silver spray. This is done with the following formula:

Stannous chloride sensitizing solution:

Stannous chloride.....	10 to 12 Gm.
Hydrochloric acid.....	5 cc.
Distilled water.....	395 cc.
Ethyl alcohol.....	600 cc.

The acid is added to the stannous chloride, then the water and finally the alcohol, and the mixture is well shaken. This mixture can be sprayed on the plastic hands, or the solution can be painted on with a brush.

Another satisfactory sensitizing solution is as follows (its disadvantages lie in its harassing effect):

Formaldehyde sensitizing solution:

Formaldehyde.....	250 cc.
Water.....	4,000 cc.

Weiss<sup>3</sup> suggested immersion for a half to one hour in a mixture made up of the following chemicals:

Stannous sulfate.....	25 to 40 Gm.
Sulfuric acid (66° Bé).....	5 to 20 cc.
Ethyl alcohol.....	120 to 250 cc.
Quinol.....	5 to 15 Gm.
Water.....	600 to 1,000 cc.

Walker<sup>4</sup> recommended a solution of the following composition:

Stannous .....	360 Gm.
Hydrochloric .....	212 cc.
Water.....	4,000 cc.

Some prefer a more dilute stannous chloride solution represented by the following formula:

Stannous chloride.....	10 Gm.
Hydrochloric acid (chemically pure).....	40 cc.
Water.....	1,000 cc.

#### FORMATION OF THE SILVER ELECTROCONDUCTIVE FILM

After the sensitizing, the hands are sprayed simultaneously with a silver solution and a reducing agent. This must be done through a dual nozzle spray gun.<sup>5</sup> The silver solution and reducing agent cannot be

3. U. S. patent 2,355,933 (Aug. 15, 1944).

4. U. S. patent 2,303,871 (Dec. 1, 1941).

5. Paasche Airbrush Company, 1909 Diversey Parkway, Chicago.

mixed until they meet on the plastic hand. The reducing agent converts the silver solution into a metallic silver deposit on the surface of the plastic.

We use the following reducing and silvering solutions:

**Reducing solution:**

Hydrazine sulfate.....	28.3 Gm.
Ammonium hydroxide.....	10 to 15 cc.
Water.....	4,000 cc.

Twenty-five cubic centimeters of the water is added slowly to the hydrazine sulfate and ammonium hydroxide until they are in complete solution.

**Silver Solution:**

Silver nitrate.....	71 Gm.
Distilled water.....	4,000 cc.
Ammonium hydroxide.....	Sufficient barely to redissolve the precipitate formed on adding the first portion of ammonium hydroxide (approximately 70 cc.)

Three fourths of the water and the silver nitrate is stirred until it is in complete solution. The ammonium hydroxide is added slowly until the solution becomes opalescent in appearance. At this point the process is continued with care to prevent the addition of too much ammonia. The amount is approximately 70 cc. Then the rest of the water is added to the mixture. The Bureau of Standards Circular Number 389 (1931)<sup>6</sup> lists three methods for producing silver films or mirrors on glass. These methods work equally well on organic plastics. However, in commercial application, a modified formulation using formaldehyde (40 per cent) as the reducing agent is being employed, with excellent results.

**Ammoniacal silver nitrate solution:**

Silver nitrate (chemically pure).....	60 Gm.
Distilled water.....	1,000 cc.
Ammonium hydroxide (28 per cent).....	60 cc.

**Reducing solution:**

Formaldehyde (40 per cent by volume).....	65 cc.
Distilled water.....	1,000 cc.

Even a little too much ammonia will prevent the silver from building up a deposit on the plastic; too small an amount will bring about an undesirable excess of precipitated oxide.

The 60 Gm. of chemically pure silver nitrate is completely dissolved in the 1,000 cc. of water. When the concentrated ammonium hydroxide is added, the mixture should be stirred constantly. The precipitate which is formed at first will redissolve when the rest of the ammonium hydroxide is added. The resulting solution, after 60 cc. of concentrated ammonium hydroxide has been added, will contain the proper amount of free ammonia for a correct silvering solution. Only

6. United States Department of Commerce, Jan. 6, 1931.

concentrated ammonium hydroxide (28 per cent; specific gravity, 0.90) should be used in this formulation. If the strength of the ammonium hydroxide has decreased on standing, a proportionate amount more must be used in the formula.

The reducing solution is made by adding 65 cc. of formaldehyde (40 per cent by volume) to 1,000 cc. of distilled water. Here again, if the strength of the formaldehyde has lessened, a proportionate increase in the amount of formaldehyde must be employed.



Fig. 1.—*A*, the spray booth for silver spraying. The air supply valve and regulating gage are to the left. On top of the cabinet are bottles of the reducing and silvering agents. These are fed by gravity to the air gun. Such a cabinet must have adequate ventilation. *B*, the dual-nosed air gun. The air is fed through the varicolored hose. The reducing and silvering agents are fed through the black hoses. *C*, as the silver is reduced, it first turns black and then white before a sufficient deposit is built up.

The spraying of the hand pattern is continued until the silver has been precipitated from the ammoniacal silver nitrate solution. It generally requires twenty to thirty minutes to produce a silver film capable of carrying current to receive an electrodeposit of metal. This point may be determined by removing a sample of the deposited mixture and testing for precipitation of silver chloride with a 10 per cent solu-

tion of sodium chloride. The silver deposit may also be tested for its conductivity with an ohmmeter or with a flash light bulb connected in series with two test prods and a dry cell battery.

After the silver spraying, the plastic pattern is rinsed thoroughly in water and allowed to dry. This may be speeded up by subjecting it to an air blast. After drying, the pattern is ready for the electrodeposition of the metal.

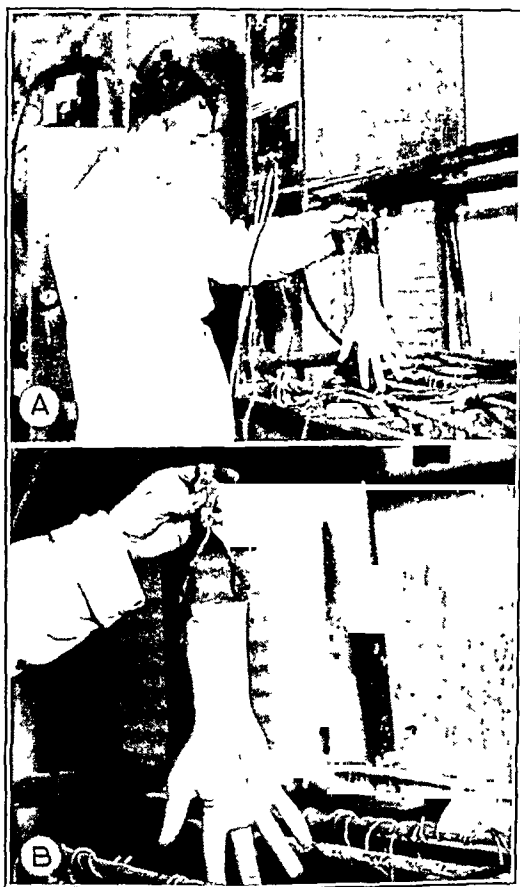


Fig. 2.—*A*, electroplating the hand. The rectifier can be seen in the top illustration. The hand is about to be put into the bath. *B*, a detail showing the battery clamp attachment to the silvered hand. The top battery clamp is attached to the cathode rod.

#### ELECTROPLATING THE PATTERN OR ELECTROFORMING THE MOLD

Electroplating or electroforming is an established and important subject about which hundreds of articles and books have been written. For the person who wishes to study the subject further, the following books are recommended: "Plating and Finishing Guidebook,"<sup>7</sup>

7. Plating and Finishing Guidebook, 11 West 42nd Street, New York, N. Y., Metal Industry Publishing Company. Published Yearly.

"Principles of Electroplating and Electroforming,"<sup>8</sup> and "Modern Electroplating."<sup>9</sup> Because of the importance of electroforming in preparing metal molds for prosthetic use, the essential facts in relation to the subject are given.

It must be realized that in forming metal molds suitable for making plastic prosthetic hands, the deposit of metal must be thicker than is accomplished in the average electroplating. Most electrodeposits can be figured in millimicrons, while the deposit suited for the metal hand molds should be between 1 and 2 mm. in thickness. Therefore, the pattern must be plated over a comparatively long period at a low voltage. This is necessary because if a high voltage is used, excessive treeing of a crystalline structure takes place. This results in a mold which lacks strength to withstand the rough treatment necessary to remove the pattern and hundreds of succeeding casts from the mold.

*The Electroforming Apparatus.*—In the past most public utilities supplied direct current power. However, today there has been a swing over to alternating current, almost to the point of extinction of the direct current. There are innumerable industrial processes and methods which can be accomplished only by means of a dependable source of direct current power. One of the greatest demands for low voltage direct current is in electrotyping and electroplating. This transition to alternating current has left a gap that had to be filled by suitable rectifying equipment.

There are two types of apparatus on the market suitable for electroplating or electroforming prosthetic hand molds. They are the electric motor generator and the variable metal plate rectifiers. While both are satisfactory, we believe that the variable metal plate rectifier is more serviceable for the following reasons:

1. It has no moving parts.
2. There is no time lag.
3. It is easy to install.
4. It is not necessary to order a unit of higher output than is needed at the time. Extra units can be added to supplement the old.
5. Because the voltage is kept between  $2\frac{1}{2}$  and 3 volts, a single unit, having an output of 75 amperes, can be used to electroform from one to five hands at the same time.

These units are capable of producing 6 and 12 volts. However, if higher voltage is used, excessive treeing will occur. Speed of electro-

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8. Blum, W., and Hogaboom, G. B.: *Principles of Electroplating and Electroforming*, New York, McGraw-Hill Book Company, Inc., 1930.

9. *Modern Electroplating*, New York, The Electrochemical Society, Columbia University, 1942.



plating is governed by a number of factors, such as the voltage employed and the temperature and concentration of the electroplating bath. Because of the low voltage employed, it requires from twenty-four to forty-eight hours to build up a hand mold of sufficient thickness to be serviceable over long periods.

*The Copper Electroforming Bath.*—We find copper to be the metal of choice. There are two main types of solutions suitable for copper plating. They are the cyanide bath and the acid bath. With the present tendency toward substantially heavier copper deposits, the acid copper bath is more important. In spite of the excellence of the cyanide bath for obtaining initial deposits, the relatively dangerous cyanide solution can be eliminated in favor of the comparatively safe acid copper bath.

These solutions must be used in enamelware, glass, crockery or rubber-lined, waterproof steel tanks. We prefer the last.

A satisfactory electroforming solution is as follows:

Copper sulfate.....	765 Gm.
Sulfuric acid.....	185 Gm.
Water.....	4,000 cc.

This bath is used under the following conditions:

Temperature.....	23.9 to 48.9 C. (75 to 120 F.)
Current density.....	15 to 40 amperes, 930.35 cm. <sup>2</sup> (1 ft. <sup>2</sup> )
Voltage.....	0.75 to 2.0 volts
Anodes.....	Rolled annealed copper

It is best that air agitation be used. This can be supplied from a small compressor and delivered into the solution through a lead pipe. In such case the bath concentration can be increased and the current density can also be raised, but not beyond 3 volts. If this is increased, unnecessary treeing of the mold and excessive polarization will occur. It is of course best to use an immersion type, electric, temperature-controlled heater in the bath during cold weather.

The following formulas, supplied by the Army Prosthetic Research Laboratory, may also be considered:

Nickel bath for initial covering:

NiSO <sub>4</sub> ·7H <sub>2</sub> O.....	70 Gm. per liter
NH <sub>4</sub> Cl.....	5.5 Gm. per liter

pH 5.8 to 6.0. Operating temperature 34 to 40 C. Current density 0.5 to 0.8 ampere/decimeter,<sup>2</sup> with air agitation

Nickel bath for heavy coatings:

NiSO <sub>4</sub> ·7H <sub>2</sub> O.....	240 Gm. per liter
NiCl <sub>2</sub> ·6H <sub>2</sub> O.....	45 Gm. per liter
H <sub>3</sub> BO <sub>3</sub> .....	30 Gm. per liter

pH 4.9 to 5.3. Operating temperature 35 to 40 C. Current density 0.8 to 1.0 ampere/decimeter,<sup>2</sup> with air agitation

Copper bath for backing up nickel:

CuSO <sub>4</sub> ·5H <sub>2</sub> O.....	200 Gm. per liter
H <sub>2</sub> SO <sub>4</sub> .....	50 Gm. per liter
Glue.....	0.01 Gm. per liter

Room temperature. Current density 1 to 1.5 amperes/decimeter,<sup>2</sup> with air agitation.

## METAL SPRAYING

Metal hand molds may be built up entirely over plastic skinform patterns by the metal spraying method alone. For this purpose, tin is the metal of choice, because the temperature of this sprayed metal is sufficiently low to prevent a blistering of the pattern during spraying. Once a deposit of suitable thickness is built up, a metal of higher melting point and tenaciousness, such as zinc or aluminum, may be sprayed over the tin. However, molds of these metals were discarded because they had discoloring effects on the vinyl chloride-acetate plastics used



Fig. 3.—*A*, metal spraying may be done in the same spray booth as silver spraying. The metal shown on the spools to the left is fed to the gun, which is held in the operator's hand. The oxygen and acetylene are provided from the tanks to the right. *B*, a close-up showing the molten metal being deposited on the skinform.

in forming the casts. The metal-spraying method produces a thicker deposit in much less time than electroforming. In fact, a mold of sufficient thickness can be built up by spraying in less than half an hour. Furthermore, this method gives sufficient detail so that the resulting hand skinform removed from a sprayed mold cannot be distinguished from the skinform removed from an electroplated mold. Unfortunately,

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the sprayed mold is crystalline in structure and will not stand the rough treatment that electroformed molds can be subjected to. We primarily use the metal spraying as an auxiliary method of quickly building up an extra deposit over the electroformed mold. In this way, thick deposits are obtained in less time than would be required by electroforming alone. However, it must be stressed that the electrodeposit must be sufficiently thick before spraying. Otherwise, sections of the two metals will separate one from the other on removal of the pattern.

The equipment for metal spraying may be purchased from any of the firms dealing in this merchandise. It consists mainly of a metal spray gun, compressor (3 horsepower or better) and a power-driven, fan-ventilated spray booth. The metal is supplied to the gun in wire form. The gases for melting the metal are provided from tanks of oxygen and acetylene. These must be rented and are returnable when empty.

#### REMOVING THE PATTERN AND MAKING DUPLICATES

Once the metal mold is finished, it becomes necessary to cut off the excess metal cuff, which has been built up by electroforming or metal spraying. This is simply cut away with a hack saw. The mold is then placed in boiling water to melt out the wax, after which it is removed and allowed to cool. After cooling, a long pair of forceps is inserted into the mold, one blade next to the mold and the other blade within the plastic pattern. The mold is then twisted as the forceps are held still. Sometimes it becomes necessary to hold the forceps with a pair of pliers or a vice. On pulling, the plastic hand pattern will either slip from the mold or be torn apart. If it tears apart, this is of little consequence, because the pattern is invariably destroyed in the process of making the metal mold or it is so discolored from the various processes that it is no longer fit for further use. Generally the palm tears from the fingers. The forceps must then be inserted into each finger, one blade next to the mold and the other within the finger, and the remaining part or parts twisted out. The mold can now be washed with water and allowed to dry.

#### SEPARATING MEDIUM

Before pouring vinyl chloride-acetate plastic into the hand, it is necessary to treat the mold with one or more separating mediums, so that the resulting cured plastics will readily separate without the excessive pulling necessary in removing the pattern.

The first separating medium we employed was a mixture of:

Silicon grease.....	50 Gm.
Carbon tetrachloride.....	950 cc.

This solution is poured from a bottle into the mold, allowed to stay for a few seconds and then poured back into the bottle. The mold is

then allowed to drain until all dripping ceases. It is then placed in an oven, with the open end up, until all the carbon tetrachloride has evaporated, leaving the thinnest coat of silicon grease on the inner surfaces of the mold. This silicon grease treatment is simple and suffices for making fifty or more plastic skinforms from a single mold before it has to be repeated.

Before the plastic is poured into the silicon grease-treated mold, it can be further treated with another silicon separating medium. This is Dow Corning Corporation's<sup>10</sup> Mold Release Fluid Number 35, which is an emulsion of silicon grease and therefore soluble in water. This is prepared in the following proportions:

D. C. Mold Release Fluid No. 35.....	250 cc.
Water.....	750 cc.

This mixture is poured from a bottle into the metal mold, allowed to remain for a few seconds and then poured back into the bottle. The mold is then hung in the oven with the open end down for draining. After drops have ceased to appear, the mold is inverted and complete drying is allowed to take place.

After complete drying, the mold is ready to receive the plastic. The first pouring of plastic should be done while the mold is cold. Where hot molds are concerned, it must be realized that the higher the temperature of the mold, the thicker will become the deposit of plastic. We find it better and advantageous to pour the plastic two or more times into the heated mold before a hand of desired thickness is obtained. Each time the mold is allowed to drain back into the original container until dripping ceases. It is then heated again for from four to six minutes in an oven of 100 C. and the pouring and draining repeated. After the final draining, the mold is placed back into an oven at 135 C. until completely cured. This takes place when all parts of the plastic have reached 135 C. and requires about ten minutes.

Some workers prefer to effect the final cure in glycerin. This is accomplished in the following manner. After the mold has been drained of plastic for the final time, it is placed in the oven for sufficient time to set the plastic. This can be determined by the fact that the inner surfaces of the cast will have lost their gloss and will no longer be sticky to touch. The mold is then removed to the hot glycerin bath, which should not exceed 150 C. Here it may remain for five minutes. The glycerin is drained from the mold, and the hot mold is placed in cold water. After complete cooling, the skinform hand can be removed from the mold without difficulty as a result of using the silicon separating medium. It is then ready for making a prosthesis for a full or partial hand.

10. Midland, Mich.

## THE PARTIAL HAND PROSTHESIS

A plaster of paris or dental stone duplicate or cast is first taken of the patient's injured member. The mold may be of either agar composition or gypsum cement (plaster of paris-water mixture). A vent must be made through the wrist, to be used later as an air escape. This is important because, in a process to be explained later, air must pass through this vent during the expansion of foam plastic.

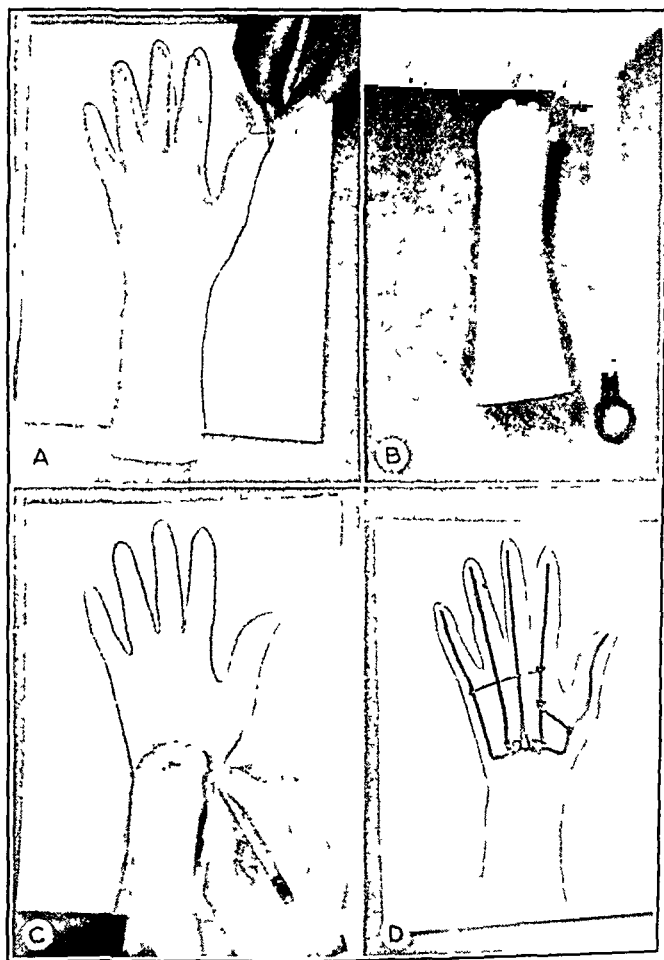


Fig. 4.—*A*, making the partial hand prosthesis. The skin form suited to the patient is chosen and its outline is traced on a piece of paper. *B*, a plaster cast of the affected or injured member with the vent former. *C*, an outline of the affected member is traced in the proper position on the paper. *D*, the wire finger armature is constructed to fit the proper space.

This vent can be created by inserting a vent former. Such an instrument may be made of stiff, 10 gage wire covered with rubber tubing. The rubber covering of the vent former is painted with a vasilin-mineral oil separator and the protruding point of the wire stuck into the center of the hand portion of the mold before it is filled with

gypsum cement. Its central position is maintained in the arm until the gypsum has set sufficiently to hold it. When the cast is completely set, the mold is removed and the vent former withdrawn. The cast is then painted with a green soap separator and set aside to dry.

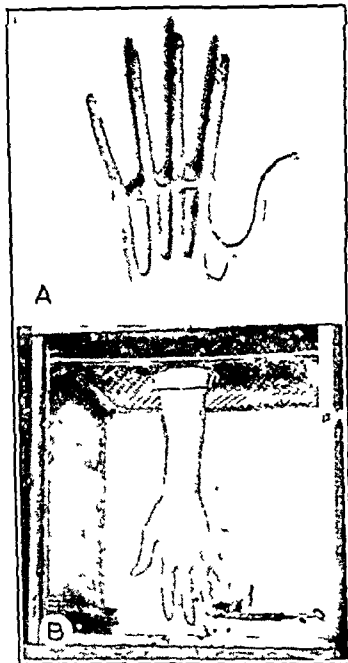


Fig. 5.—*A*, the wire armature after dipping in plastic. *B*, the wire armature is put in place in the skinform. The foam is added, and the plaster cast of the affected member is inserted. The composite casts are placed in the oven for expanding the foam

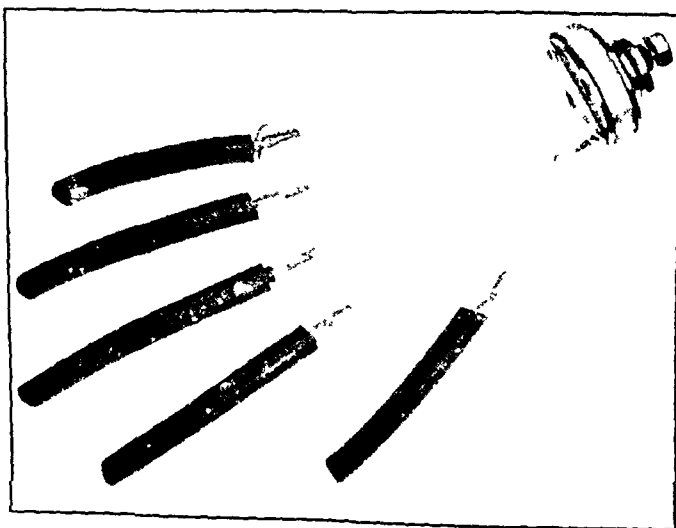


Fig. 6.—*A*, a wire rubber methyl methacrylate armature, devised by the Prosthetic Laboratory of the Veterans Administration for using in the skinform for total hand prostheses. The foam is applied between the armature and the skinform.



The cosmetic glove or skinform selected for its similarity in size and character to the patient's unaffected hand is laid on a piece of white paper and carefully traced in pencil. Next the patient's injured hand or the plaster cast is placed on this tracing, and the line indicating the extent of his loss is traced. With the area to be filled or replaced reduced to a line drawing, the next step in making a necessary wire skeletal device becomes much easier. This wire frame or skeletal device is made to provide the missing fingers with the necessary

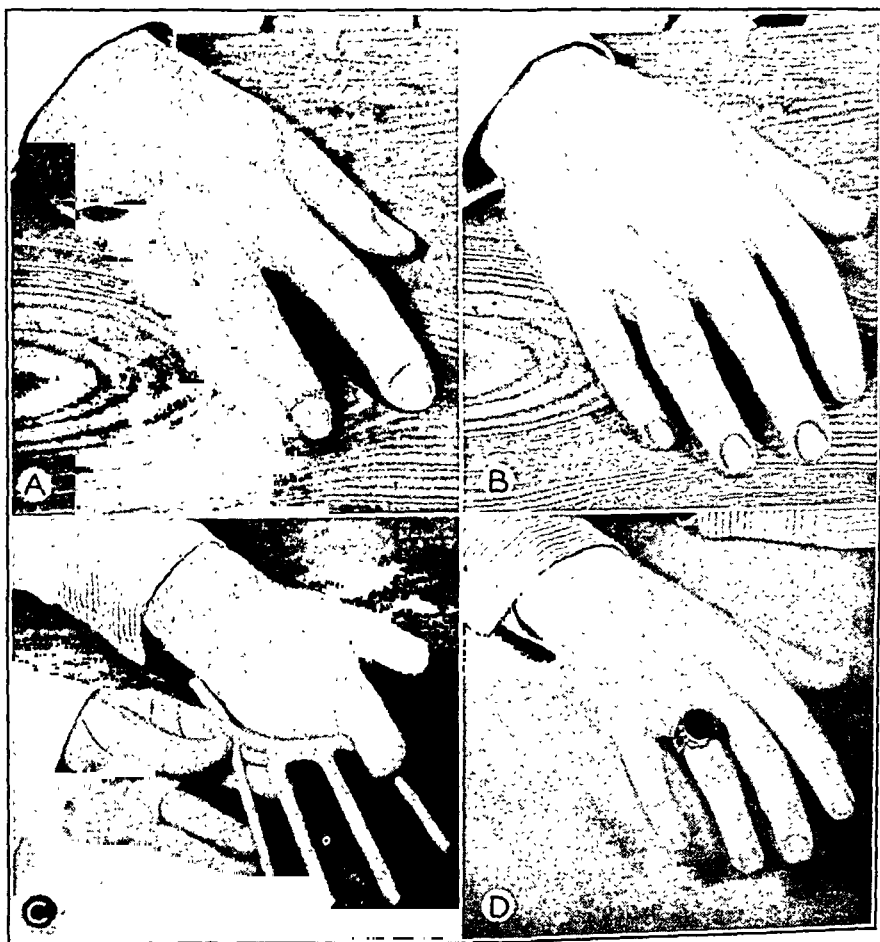


Fig. 7.—*A*, an affected member. *B*, the completed plastic prosthesis on the patient. *C*, an affected member, showing the plastic-covered armature in place. *D*, the completed plastic prosthesis on the patient.

rigidity and to allow for flexibility, so that the patient may bend the fingers with the good hand to any desired position, permitting gripping and holding. This wire frame should extend as far as possible into the palmar area to insure a proper change of plane at the knuckles when the hand is cupped or made into a fist. The device is made of 8 gage copper wire, flattened and soldered with acid core solder if

more than two fingers are to be replaced. The flattening is accomplished by using an anvil and ball peen hammer. The portions to be soldered are then sanded and bound with fine copper wire. After completion, the soldered device is next heated over a gas stove flame and dipped while hot in a vinyl plastic. Here it is allowed to remain for two



Fig. 8.—*A*, the affected member. *B*, the natural hand being clasped with the prosthesis. *C*, the inner surfaces of the prosthetic and the natural hand for comparison.

minutes to build up an insulating coat or deposit. On draining, it is cured for half an hour at 100 C. and is ready for a trial fit.

The plastic-covered metal skeletal device should be trial fitted in the skinform with the cast of the patient's hand in place. The skeletal fingers should extend to the tips of the glove to insure their bending to

the last joint. However, if any finger of the skeletal device is long enough to stretch the skinform, the offending tip should be pared down with a pair of pliers or scissors or a sharp knife until no tension is apparent. This is to prevent possible breaking as a result of stress during curing.

For filling the area between the hand skinform and the plastic-covered metal skeletal device, we have found foam plastic satisfactory. Before the foam may be used, however, it is important that all curing glycerin be removed from the inside of the skinform to insure the foam adhering to the inside surfaces. In addition to thorough washing, a 2 to 6 per cent dilution of amyl alcohol or cyclohexanone may be added to the foam plastic. For best results the foam plastic should be mixed with from 1 to 2 per cent of water just prior to use. The fingers of the skinform corresponding to the missing digits of the cast of the patient's hand are filled with the liquid foam plastic. The wire frame is then inserted into the skinform and rechecked to insure that it extends to the finger tips. This is done to insure automanipulation of the finished prosthesis to the distal phalanges. Next the prepared plaster cast of the patient's partial hand is inserted in the wrist opening. These are hung in the oven by a wire attached to the wrist of the cast. The temperature of the oven should be started at 70 C. and gradually increased to 100 C. This temperature should be maintained for three quarters of an hour before the hand is removed. The reason for the low starting temperature is to allow the foam time to expand fully before setting. If the heat is regulated correctly, the volume of the foam will be doubled on curing. On removal from the oven, the filled skinform is allowed to cool thoroughly before the cast is removed. When this has been done, the prosthesis is ready for coloring and fitting on the patient. Coloring has been explained in detail in the book "Facial and Body Prosthesis."<sup>11</sup>

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## ORIGINS OF THE NATIONAL AND REGIONAL SURGICAL SOCIETIES

Presidential Address

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THE MIDDLE of the nineteenth century was a notable epoch in the chronicles of American medicine. The demonstration of ether anesthesia to a medical group in 1846 was followed by the rapid development of the medical sciences, particularly cellular pathology, bacteriology, organic chemistry and experimental physiology. Through the application of the knowledge derived from the basic sciences to clinical practice, medicine gradually emerged from the age of theories and systems and assumed its position as one of the major disciplines of biology. Furthermore, attempts to regulate certain aspects of medical practice were introduced during this period. In 1847, the American Medical Association was founded, chiefly for the purpose of improving the state of medical education but also to combat the evil of college faculties' both teaching and licensing medical students. In 1860, the scientific sessions of this body were divided into four sections, one of which was surgery. For some twenty years this surgical section of the American Medical Association was the only national forum at which physicians from all parts of the country interested in surgery could convene, exchange views and compare experiences. Surgery at that time was almost static; its scope was limited, there were no surgical specialists and all surgeons were general practitioners. The attendance at these yearly meetings of the surgical section was large, since it was purely voluntary, and no attempts were made to limit participation to those having special qualifications in surgery.

It was not until Lister succeeded in transferring the discoveries of Pasteur to the management of surgical wounds that elective operations within the abdominal cavity, the thoracic cage, the cranial chamber and the joints were made possible. With the field of surgical endeavor thus enlarged, the number and variety of surgical operations in all hospitals increased at a rapid rate and ingenious surgeons were quick to devise new procedures and when necessary to discard or modify the older

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Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

ones. Knowledge of surgery thus accumulated rapidly, although the opportunities for this type of surgical education were not available equally to all. Those most fortunate in this respect were the chiefs of the surgical clinics in the large hospitals, then situated for the most part along the eastern seaboard. These men, having the control of clinical material, were able to amass a vast amount of information and by thoughtful study to formulate well considered opinions and to chart new fields for exploration. Certain of these physicians in the vanguard of surgical progress foresaw the advantages to be gained through the establishment of special national organizations comprising a restricted number of physicians from different parts of the country having a common purpose and working under similar conditions.

Such a man was James Read Chadwick (1844-1905), of Boston, best known to succeeding generations of medical students and physicians through the eponym, Chadwick's sign of pregnancy. Chadwick, surgeon, bibliophile, collector, teacher and humanitarian, after graduation from the Harvard University Medical School in 1871, spent two years abroad studying in Berlin, Vienna, Paris and London in accordance with the custom of the day. Early in his career, he evinced special interest in the then new specialty, gynecology, and on entering practice became gynecologic surgeon to the Boston City Hospital. It was he who, while still a young man, conceived the idea of a small national association to be composed of representative men whose reputations in the field of obstetrics and gynecology were already established. He believed the centennial year to be a propitious time for the founding of such a society, and, accordingly, with the assistance of J. Tabor Johnson, Paul Munde and E. R. Peaslee, he formulated a plan for an American Gynecological Society. An organizational meeting was held in New York, June 3, 1876. At this time it was agreed that the society should have a restricted membership and that the qualifications of candidates for admission should be high. It was believed that thereby membership "would be coveted and sought after and the discussions would be more profitable." The first annual meeting was held in New York, Sept. 13, 14 and 15, 1876, with Fordyce Barker the first president and Chadwick the first secretary, an office which he held for seven years. By virtue of his ability, commanding personality and tact, Chadwick did much to secure able men as a nucleus for the organization and to maintain the high ideals set by the founders. At first, membership was limited to sixty, this number later being increased to one hundred. The original constitution gave as the object of the society, "the promotion of all that relates to the diseases of women and to obstetrics," while subsequently the phrase "and to abdominal surgery" was added. In the beginning, the council voted to publish yearly

transactions of the meetings and with the assistance of John Shaw Billings, then in charge of the National Medical Library in Washington, to append to each volume a complete bibliography of all of the literature pertaining to obstetrics and gynecology of that year. In the early years of the society, candidates for admission were required to present to the executive council a paper embodying original work of either a clinical or an experimental nature. The papers of those candidates elected to membership were published in a special section of the following volume of the transactions.

The motto selected for the society was the following quotation from Goethe:

Wie das Gestirn  
Ohne Hast  
Aber ohne Rast  
Drehe sich jeder  
Um die eigene Last

Without question, the most eminent surgeon of his time was Samuel David Gross (1805-1884), of Philadelphia. A peerless surgeon endowed with a sterling character, a benevolent disposition and dignified mien, and possessing a profound knowledge of his subject, he was one of the most inspiring and influential teachers of his day. Born of German parents in Easton, Pa., Gross received both his preliminary and his professional education in America. After graduation from the Jefferson Medical College of Philadelphia in 1828, he held teaching positions in the medical schools of Ohio, Cincinnati and Louisville, finally returning to his alma mater in 1856 as professor of surgery. He was a scholarly and prolific writer in the fields of both clinical and experimental surgery and played an important role in the development of surgical pathology. His "Elements of Pathological Anatomy" in two volumes, published in 1839, was one of the classics of his time.

With his customary broad vision, Gross believed that among the sixty thousand physicians in the United States, there was a group of surgeons whose professional skill and ability as teachers and writers was such that their organization into a national association would be of distinct advantage and that this would serve "to embody in one harmonious whole, the surgical talent and wisdom of this great country." Accordingly, with the aid of his close friends, Moses Gunn, William T. Briggs and William W. Dawson, his plan for an American Surgical Association was brought before the members attending the surgical section of the American Medical Association at its meeting in Atlanta, Ga., in May 1879. The idea of such an annual consultation of surgeons met with favorable response, and, accordingly, the principal surgeons of the United States were invited to attend an executive session the next year, again at the time of the meeting of the American Medical Association.

At this time Gross was elected the first president, which office he held until 1884, when he was succeeded by Edward M. Moore. He has the unique distinction of being the only member ever to serve as president for more than one year. A final preliminary meeting was held in May 1881, followed by the first scientific session at Coney Island four months later. The first volume of the transactions was published in 1883 and contained the reports of the first three regular meetings. According to the original constitution, the number of members was limited to one hundred. In 1883 an amendment raising this to one hundred and fifty failed to pass because it was feared the association would become unwieldy. Later, however, this amendment was adopted. No further change occurred until 1934, when the limit was raised to one hundred and seventy-five, and only very recently has this been increased to two hundred and fifty. In accordance with the original custom, the annual meetings continue for three days and are held in the late spring, a time originally chosen in order to follow the termination of the school year. The official seal of the association bears the profile of Samuel Gross.

Prior to the turn of the century, there were few surgeons who restricted their work to urology, although important contributions in this field had been made by such men as Bigelow, Arthur Tracy Cabot, Van Buren, Fuller, Gouley and others. Genitourinary surgery at that time was concerned chiefly with disorders of the male urethra and prostate and occasionally with bladder stone, and it was often combined with syphilology. Edward Lawrence Keyes (1842-1924), one of the leading genitourinary surgeons of his day, did much to clarify the status of urology and to elevate it to the dignity of an independent surgical specialty. Much of his influence was exerted through a textbook published in 1874 and entitled, "A Practical Treatise on the Surgical Diseases of the Genito-Urinary Organs Including Syphilis," of which he was co-author with Van Buren. Educated at Yale and the New York University Medical College, Keyes then spent a year in Paris studying dermatology. On his return to New York, he was appointed professor of dermatology in the Woman's Medical College of the New York Infirmary for Women and Children. He later became professor of dermatology, syphilology and genito-urinary surgery at the Bellevue Hospital Medical College, and at the Bellevue Hospital he unofficially established what was probably the first urologic ward in this country.

In view of his admirable achievements as a teacher, clinician and investigator, it was logical that he should have been the founder of the American Association of Genito-Urinary Surgeons. On Oct. 16, 1886, at the invitation of Keyes, a meeting was held at 1 Park Avenue for the purpose of organizing a society to be devoted to the study of genito-urinary and venereal diseases. At this meeting, at which there were

eleven guests, mostly from Boston and New York, the necessity for and advantages of such an association composed of surgeons from the several parts of the country were discussed. It was agreed that the study of syphilis should be included in the proposed work of the society. Keyes was elected the first president. The first annual meeting was held at Lakewood, N. J., May 17 and 18, 1887, and the papers presented at this session were subsequently published in the *Journal of Cutaneous and Genito-Urinary Diseases*. From the first, urologic subjects dominated the programs and during the ensuing twenty-five years papers pertaining to venereal disease and syphilis gradually diminished in number and the interests of the group finally became concentrated on problems in urologic surgery. It was not until 1907 that the publication of yearly transactions of the association was begun. The number of members according to the original constitution was limited to fifty, although in 1905 this was increased to sixty.

The idea of an American Orthopedic Association and plans for such were evolved independently by Newton M. Shaffer (1846-1928) and Virgil P. Gibney (1847-1927), of New York. Both of the founders were pioneers in the field of orthopedic surgery, and both had long and distinguished records of service at the Hospital for the Ruptured and Crippled. The plans of these two men were consolidated at a meeting at the home of Shaffer on Jan. 29, 1887, when a group of men interested in the subject was invited to consider formally the formation of such an organization. It was agreed that there was need for this type of an association, first, to bring together American orthopedic surgeons and, second, to secure better recognition in Europe of American orthopedic surgery. Plans for the organization were drawn up, and the first annual meeting was held at the Academy of Medicine in New York, June 15 and 16, 1887, when Shaffer was honored by being made the first president. The aim of the organization as given in the constitution was the advancement of orthopedic science and art. Members were to be graduates in medicine, in good professional standing and especially interested in orthopedic surgery. Candidates for admission were to have been in the practice of medicine for at least three years and should have given evidence of satisfactory scientific attainment. There were thirty-five names on the original roster of members. In 1890, a proposed amendment limiting the number of members to fifty was voted on and lost. At the present time, the number is not to exceed two hundred. For fifteen years the transactions were published annually. Beginning in 1903 this was discontinued, and papers presented at the meetings were published in the new *American Journal of Orthopedic Surgery*, a periodical published by the Association, which replaced the transactions.

It is of interest that in 1888 a second national society in the field of obstetrics and gynecology was formed. This organization came into



existence largely because of the efforts of Albert Vanderveer (1841-1929), then professor of clinical, didactic and abdominal surgery in the Albany Medical College, and of W. W. Potter (1838-1911), of Buffalo. The reasons for the formation of this society were set forth by Adam H. Wright in his presidential address in 1891, when he recalled that in 1886 the Congress of American Physicians and Surgeons had been organized and was designed to serve as a federation embracing all the organized special societies. Its by-laws stated that the congress should be composed of national associations for the promotion of medical and allied sciences and that it should hold its sessions triennially in the city of Washington, D. C. Obstetrics and gynecology was the only important specialty not represented at that time. Friends of the congress believed that if a society in this field were properly organized it would obtain admittance to the congress. Accordingly, an invitation was issued to certain men representative of abdominal surgery, obstetrics and gynecology in various parts of the United States to assemble and consider the wisdom of effecting such an organization. Fifteen men gathered at "The Niagara" in Buffalo, on April 19, 1888. Plans for the formation of the American Association of Obstetricians and Gynecologists were completed, and the first annual meeting was held the following fall. While this organization was not subsequently admitted to the congress, as had been hoped and planned, nevertheless a flourishing society came into existence and it has continued through the years to have contributed greatly to the expansion of the general fund of knowledge in this special domain. The membership was originally restricted to one hundred, whereas at the present time it is set at one hundred and fifty. From the beginning, an annual transactions has been published, and since 1920 the *American Journal of Obstetrics and Gynecology* has been the official organ of both this association and the American Gynecological Society. In 1920 the name of the society was changed to the one used at present, the American Association of Obstetricians, Gynecologists and Abdominal Surgeons.

With the increase in the scope and importance of surgery following the advent of the aseptic method, the educational value and constructive work of the national surgical societies were convincingly demonstrated. However, because of their restricted membership and the fact that they were dominated by the large medical centers of the East, many able men in other sections of the country, particularly in the South and the West, were denied the stimulation, the social advantages and educational value of such meetings. Moreover, travel at that period was time consuming and difficult. It naturally followed that the demands and needs of these groups were met by the further extension of organized surgical societies in the form of sectional or regional organizations having a pattern similar

to that of the older national groups. Two of the earliest and best examples of this trend are to be found in the origins of the Southern Surgical Association and of the Western Surgical Association.

The Southern Surgical Association came into existence through the earnest and untiring efforts of William E. B. Davis (1863-1903), of Birmingham, Ala. Davis, early in his medical career, chose abdominal surgery and gynecology as his chief field of interest, and he held the chair of gynecology and abdominal surgery in the Birmingham Medical College, of which he was a founder. In order to provide the surgeons of his locality with the advantages to be derived from participation in surgical meetings of a high order, in 1886 he became the organizer of the Surgical and Gynecological Society of Alabama, despite considerable opposition by many of his colleagues. This organization had a brief existence, as its first and only meeting was held in October 1887. However, from it stemmed the Southern Surgical and Gynecological Association, a more comprehensive society, plans for which were considered at this 1887 meeting. W. D. Haggard Sr., the first president, in his annual address, pointed out that the Southern Association was not intended to remain purely sectional in character but that prominent surgeons from other parts of the country were to be invited to meet with the surgeons of the South for the exchange of ideas and discussion of experiences and to encourage the undertaking of and reporting of original work, especially by the younger men. The region served included the eleven original Southern states and also Kentucky, Maryland, Missouri and the District of Columbia. By tradition, all officers have been residents of these states, and with but two exceptions no meetings have been held outside of this Southern territory. Although originally there was no constitutional limit to the number of members, it was the intention of the founders to restrict the membership to one hundred. By 1891, however, because of the rapid growth and popularity of the association, it became necessary officially to limit it to one hundred and fifty, and in 1902 this number was advanced to two hundred, where it has remained. In 1917 the name of the organization was changed to the Southern Surgical Association. Nevertheless, papers in the field of gynecology have continued to appear on the programs and this specialty is represented by an appreciable number of members. A permanent record of the meetings has been preserved in the annual transactions. A miniature portrait of Ephraim McDowell of ovariectomy fame constitutes the official seal of the organization.

In the early nineties of the last century, the western part of the United States was relatively undeveloped and methods of communication and transportation were primitive. For these reasons a group of men, most of them obstetricians and gynecologists, concurred in the idea

that a society composed of surgeons residing in the Western states which would meet at some point accessible to most of them would be desirable. Credit for developing this idea into a realization goes to Milo B. Ward (1848-1901), one of the prominent gynecologists of Topeka, Kan., and a pupil of Joseph Price, of Philadelphia. At Ward's invitation the group convened in Topeka on Oct. 5, 1891, made preliminary plans and adopted the name, The Western Association of Obstetricians and Gynecologists, presumably because the greater part of the surgery of that period was of this type. In December 1891, the first regular meeting was held in Topeka, when the details of organization were completed and Ward was chosen the first president. According to the original plans, the members were to be men who were giving special attention to the practice of obstetrics and gynecology and who resided in the Missouri River cities of Iowa and Missouri and the states of Kansas, Nebraska, Colorado, New Mexico, Indian Territory and Oklahoma. Since then the territory covered by the Association has been enlarged so that all the Western states are now included. The earlier programs were published somewhat sporadically, usually in the *Journal of the Kansas Medical Society*. Beginning in 1897, the record of this entire meeting was published in book form as a transactions, and that policy has been continued to the present time. Gradually the topics of papers presented included more and more subjects of a general surgical nature, and in 1895 the title was changed to the Western Surgical and Gynecological Association. This persisted until 1909, when it became The Western Surgical Association. Originally, membership was limited to one hundred. In 1903 this was increased to one hundred and fifty, in 1929 to one hundred and seventy-five and in 1948 to two hundred.

Shortly after the turn of the century, some of the more ambitious and enthusiastic younger surgeons became dissatisfied with the existing policies of medical societies and the conduct of medical meetings. They resented the ultraconservative, exclusive and inflexible policies of the older surgical societies with regard to the admission of younger men to membership and also the formality and pedantic didacticism which characterized some of the programs. Since the prevailing order, strengthened by long tradition, could not easily be altered, a small number of this rebellious younger group, all holding university positions, decided to form a new society, the activities of which would be conducted along entirely different lines. Cushing related that possibly the idea of a clinical surgical society was first discussed by W. J. Mayo, A. J. Ochsner and himself in 1900 while they were attending the Twelfth International Medical Congress in Paris. However, it remained for George Crile

(1864-1943) to take the initiative in the actual formation of such a new society, and, accordingly, he and James Mumford invited a small group of their colleagues to meet in New York for the purpose of organization. On July 11, 1903, at the Murray Hill Hotel, the Society of Clinical Surgery was officially founded. The original members included George Crile, James G. Mumford, John C. Munro, Charles H. Frazier, George E. Brewer and Harvey Cushing. Most of these men were then in their thirties, and the age for retirement from active membership was set at 55. Crile formulated a plan for the conduct of the meetings which comprised his seven commandments. In summary these were: 1. No formal papers should be read. 2. Nothing presented at a meeting was to be published. 3. The meetings were to be in the form of demonstrations and to be held at the hospital where the surgeon entertaining the society worked. 4. Business sessions and entertainment were to be kept to a minimum. The aim of the society, according to Crile, was "a minimum of proceedings and a maximum of ideas—a 'show-me' society for mutual benefit." The first regular meeting was held in Baltimore and Philadelphia, Nov. 13 and 14, 1903, with J. M. T. Finney the first president. Originally it was planned to have two two day meetings a year, each meeting to include operative clinics in two neighboring cities, such as Baltimore and Philadelphia, New York and Boston, Cleveland and Buffalo and Chicago and Rochester, Minn. Later it was deemed advisable to hold the two day program in one city. Having made a complete circuit of the United States twice, the first meeting abroad was held in 1910, the visit including the medical centers of the British Isles, where in Great Britain a similar organization, the Provincial Surgical Society, had been formed. Membership in the Society of Clinical Surgery is limited to fifty. This method of informal clinical demonstrations has met with great success, and this society has served as the prototype for many similar organizations or travel clubs, not only in surgery and the surgical specialties but in other fields of medicine as well.

Franklin H. Martin (1857-1935), managing editor of the journal *Surgery, Gynecology and Obstetrics*, which had been established in 1905, impressed by this dramatic method of objective presentation of clinical work, conceived the idea of utilizing such a plan for adult education, on a much larger scale in order to make available to the great group of practicing surgeons the advantages theretofore possible for only a few. At his instigation, the editorial board of *Surgery, Gynecology and Obstetrics* arranged for a group of surgical clinics to be given in Chicago from Nov. 7 to 19, 1910, to which it invited subscribers to the journal. The attendance was large and the success of the venture phenomenal, so much so that those attending the clinics expressed a

desire to perpetuate them. Accordingly, a meeting on permanent organization followed and the name The Surgical Congress of North America was selected. As the popularity of the congress continued during the ensuing years, it became evident that it would be necessary to exercise some control and to limit attendance at the clinics to the registered surgeons and to choose wisely the clinics and clinicians invited to participate. This, in turn, led to the plan of Franklin Martin for a new organization closely allied with the congress through which definite qualifications for membership would be established, thereby elevating the standards of surgery. On May 5, 1913, the American College of Surgeons was officially founded, and in 1917 the two organizations were amalgamated.

With the application of surgical methods to the treatment of disorders of the chest, a new specialty, thoracic surgery, evolved in the early years of the present century, and developments in this field were considerably accelerated by the experiences gained in World War I. The real founder and dean of this specialty in America was Willy Meyer (1858-1932). Born and educated in Germany, Meyer at the age of 26 came to New York, where he had a long and remarkable surgical career. Always intensely interested in the various aspects of cancer, he devised an original plan of radical mastectomy for mammary carcinoma. Unknown to Meyer, Halsted, who had been working on the same problem for a longer time, independently developed an almost identical procedure and anticipated Meyer in the reporting of his results. Realizing the great possibilities for thoracic surgery in the future, in February 1917, Meyer invited twenty New York physicians to meet in his office for the purpose of organizing the New York Society for Thoracic Surgery. One of the purposes of this organization was to lay the foundation for an American Association for Thoracic Surgery. At the next meeting of the American Medical Association, in New York city, June 7, 1917, members of the New York Society invited the leading thoracic surgeons of the country to be their luncheon guests, and at that time the American Association for Thoracic Surgery was officially organized with fifty founder members. Samuel Meltzer, of the Rockefeller Institute, was chosen the first president.

A significant event in the history of this surgical organization has been a deviation from the older policy of limiting membership to surgeons alone. Here, on the contrary, internists, radiologists, endoscopists and others working on thoracic problems in the laboratories of physiology, pathology and bacteriology have been welcomed to membership. Secondly, a novel feature in organization has been the group of associate members in addition to the active, senior and honorary members. These

men are elected for a limited period (five years). During this time an associate member, if properly qualified, may be elected to active membership. At the expiration of this limited period, if not yet qualified for active membership, an associate must either be reelected as such for an additional period or be dropped.

Finally, this new surgical organization, with high standards, stimulating meetings and an outlet of its own for publications, made possible membership to a number of the well trained younger general surgeons who were working in the thoracic field and who were desirous of such an affiliation but who were not yet eligible for membership in the older societies.

In September 1912, Harvey Cushing (1869-1939) became the third Moseley Professor of Surgery at Harvard, succeeding Maurice H. Richardson in this the oldest of the endowed surgical chairs. At the same time he became the first surgeon-in-chief at the new Peter Bent Brigham Hospital. Cushing's pioneer work in the surgical treatment of diseases of the nervous system is too well known to warrant recounting here. Being a firm believer in the importance and educational value of medical meetings, at the time of the clinical congress of the American College of Surgeons in New York in 1919, Cushing proposed to some of his colleagues the formation of a neurosurgical travel club. Thereby as a group they could visit one another at their respective clinics, the meetings to be held once or twice a year. The idea was enthusiastically welcomed, and with ten charter members "The Neurosurgical Club" was formed. These original members were A. W. Adson, Charles Bagley Jr., Harvey Cushing, Charles E. Dowman, Charles A. Elsberg, Charles H. Frazier, Samuel C. Harvey, Gilbert Horrax, Dean Lewis and Ernest Sachs. In March 1920, a meeting was held at the Peter Bent Brigham Hospital, at which time the original name was abandoned and The Society of Neurological Surgeons was officially founded. The first clinical meeting was also held in Boston, Nov. 26 and 27, 1920. The general plan has been similar to that of the Society of Clinical Surgery, an organization in which Cushing throughout his life maintained a deep interest. At each meeting one or more members act as hosts at the hospital where they work. The meetings are held in rotation at the various neurosurgical centers. The number of members has not exceeded forty.

A generation of surgeons has come and gone since Chadwick and Gross and Keyes and Shaffer first disclosed to their intimate friends their visionary plans for a particular national surgical society. During this period of nearly seventy-five years, the population of the country has increased almost threefold and the number of physicians has so multiplied that according to the most recent calculations there is now

in the United States one doctor for every seven hundred and ten persons. Nevertheless, the original restrictions on the size of the senior societies have been adhered to almost literally, and presumably owing to reverence for the wishes of the founders, enlargement of the membership has been jealously guarded. With the passing of the years, the requirements for admission have become more and more stringent, and a candidate must, therefore, be more or less well known and must give evidence of having made some contribution to the advancement of the art and science of surgery. As a result, most of the successful aspirants have reached at least early middle age, and election to membership, often beset by delays, not infrequently comes as a *cum laude* award in recognition of a considerable part of their life's work. Because of the emphasis placed on investigation and education, most of the members hold responsible positions in the medical schools. In reviewing the achievements of these organizations, it is difficult or impossible to estimate fully the value of the benefits which have been derived from the combined efforts of the best medical minds in the country concentrating on their particular scientific problems and working for a common cause.

The three quarters of a century just past has witnessed, in addition to the increases in population and number of physicians, a remarkable increase in the number of hospitals and of well trained surgeons. The latter advance has been due chiefly to the more general adoption by hospitals of the residential system, a German method of graduate training originally transplanted to this country by Halsted and Osler in the early days of the Johns Hopkins University. The junior surgeon of today who has attained and held the post of resident surgeon has, at the age of 30, had an experience in surgery which in the case of many of our distinguished forebears could scarcely have been accumulated during a lifetime of practice. The Central Surgical Association hails these junior surgeons, as for them it was conceived and founded, and in welcoming them to membership it endeavors to offer them the opportunities and privileges with the dignity which they deserve. On the shoulders of these younger surgeons now fall the tasks and duties originally assumed by the founders and founder members. As they take over the responsibility for guiding the destinies of the Association in the future, we can do no better than to restate with slight modification the words of Samuel Gross written nearly seventy years ago when he expressed his hopes for the future of the Association which he founded: "to foster surgical art, science, education and literature, to cultivate good feeling in the profession and to unite prominent surgeons of the country in one harmonious body."

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# PHARYNGEAL NEURILEMMOMAS OF CRANIAL NERVE ORIGIN

Medial Displacement of the Internal Carotid Artery as a Diagnostic Sign

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AND

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FOUR patients with tumors of the upper cervical cranial nerves have been studied. All the lesions were neurilemmomas, 3 arising from the vagus nerve and 1 from the hypoglossal. All 4 cases presented a syndrome consisting of dysphagia due to pharyngeal compression and pulsation of the tumor due to medial displacement of the internal carotid artery. In addition, there was a paralysis of the vocal cord on the same side in 2 of the patients whose tumor arose from the vagus nerve. This triad of findings enabled us to make a clinical diagnosis of the lesion in the last 2 patients. The cases are being reported because, as far as we can ascertain, this syndrome has not previously been described.

The neurilemmoma is not a common tumor, but it is by no means rare. The importance of these lesions lies in the fact that, whereas they are benign encapsulated tumors which are resectable and surgically curable, they are not infrequently confused with malignant lesions carrying a much worse prognosis. In such instances, patients may be subjected to unnecessarily mutilating surgical procedures, such as amputation of an extremity or an ill advised radical resection or to intensive radiation therapy, or they may be refused treatment for a lesion which is completely curable. These considerations are especially pertinent to neurilemmomas arising in the region of the head and neck, where they are relatively inaccessible, where differential diagnosis includes many clinical entities and where pressure effects of a benign tumor may be serious, owing to obstruction of airway, food passages and circulation. Although a neurilemmoma may arise from the sheath of Schwann of a nerve anywhere in the body, according to Ehrlich and Martin<sup>1</sup> about half of all these tumors surveyed were

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From the Department of Surgery, University of Illinois, College of Medicine, the Illinois Research and Educational Hospitals, and the Presbyterian Hospital.

1. Ehrlich, H. E., and Martin, H.: Schwannomas (Neurilemmomas) in the Head and Neck, Surg., Gynec. & Obst. **76**:577, 1943.

found in the head and neck region, the majority being cervical in location. In only 26 per cent of Stout's series of 50 cases was the tumor found above the clavicles.<sup>2</sup> Ten neurilemmomas have been reported arising specifically from cranial nerves in the cervical region,<sup>3</sup> involving the pharynx. Many cases have been reported in which these tumors arose in the head and neck.

The nomenclature of these benign encapsulated neurogenic tumors is varied, resulting in confusion. Described and termed neurinoma in 1910 by Verocay,<sup>4</sup> subsequent writers have referred to this tumor as a perineural fibroblastoma,<sup>5</sup> neurilemmoma,<sup>6</sup> schwannoma,<sup>7</sup> neurofibroma<sup>8</sup> and peripheral glioma.<sup>9</sup> The terms neurilemmoma and schwannoma are most frequently used, and, since the former seems to be the most accurate designation, it is used here to designate those tumors which have their origin from the neurilemma of cranial and peripheral nerves. Theoretically, neurilemmomas may arise in any part of the body, although they are most frequently found in the cervical region, where the cranial nerves and sympathetic system with cervical plexiform rami are abundant. The anterior aspect of the extremities is the next most frequent location after the cervical region.

2. Stout, A. P.: The Peripheral Manifestations of the Specific Nerve Sheath Tumor (Neurilemmoma), *Am. J. Cancer* **24**:751, 1935.

3. (a) Turchik, F.: Schwannoma of the Pharynx with Paralysis of the Vocal Cord, *Arch. Otolaryng.* **44**:568 (Nov.) 1946. (b) Cutler, E. C., and Gross, R. E.: Neurofibroma and Neurofibrosarcoma of Peripheral Nerves, *Arch. Surg.* **33**:733 (Nov.) 1936. (c) Nigro, A., cited by Turchik.<sup>3a</sup> (d) Murray, M. R.; Stout, A. P., and Bradley, C. F.: Schwann Cell Versus Fibroblast as the Origin of the Specific Nerve Sheath Tumor, *Am. J. Path.* **16**:41, 1940. (e) Bustos, F. M.: Schwannoma of the Pneumogastric Nerve: Case with Recovery after Ablation, *Bol. y trab. Acad. argent. de cir.* **29**:448, 1935. (f) Sekiguchi, S., and Oije, T.: *Arch. f. klin. Chir.* **143**:113, 1926, cited by Ehrlich and Martin.<sup>1</sup> (g) Murley, R. S.: A Case of Neurinoma of the Vagus Nerve in the Neck, *Brit. J. Surg.* **36**:101, 1948. (h) Friedman, L., and Eisenberg, A. A.: Neurofibroma of the Hypoglossal Nerve, *Ann. Surg.* **101**:834, 1935. (i) Ehrlich and Martin.<sup>1</sup>

4. Verocay, J.: Multiple Geschwuelste als Systemerkrankung am nervoesen Apparate, *Festschr. f. Mans Chiari*. . . seines 25 jähr. Prof.-Jubil., Wien u. Leipz, 1908, p. 378; *Beitr. z. path. Anat. u. z. allg. Path.* **48**:1, 1910.

5. Mallory, F. B.: The Type Cell of the So-Called Dural Endothelioma, *J. Metab. Research* **4**:349, 1920. Penfield, W.: The Encapsulated Tumors of the Nervous System, *Surg., Gynec. & Obst.* **45**:178, 1927.

6. Ewing, J., cited by Ehrlich and Martin.<sup>1</sup> Stout.<sup>2</sup>

7. (a) Violé, P.: Schwannoma of the Pharynx, *Ann. Otol., Rhin. & Laryng.* **55**:334, 1946. (b) Koop, C. E.; Jordan, H. E., and Horn, R. C.: Schwannoma of the Pharynx, *Surg., Gynec. & Obst.* **85**:641, 1947. (c) Turchik.<sup>3a</sup>

8. (a) Figi, F. H.: Solitary Neurofibroma of the Pharynx, *Arch. Otolaryng.* **17**:386 (March) 1933. (b) Hall, C., and Owens, H.: Solitary Neurofibroma of the Pharynx, *ibid.* **34**:1163 (Dec.) 1941. (c) Cutler and Gross.<sup>3b</sup>

9. Masson, P.: Experimental and Spontaneous Swannomas (Peripheral Gliomas), *Am. J. Path.* **8**:367, 1932.

Pharyngeal neurilemmoma is relatively uncommon. New and Childrey<sup>10</sup> collected from the Mayo Clinic 63 cases of benign tumors of the pharynx and tonsil over a thirteen year period (1917-1930). In this relatively large group of benign tumors, a primary neurilemmoma of the pharynx was not encountered. Koop, Jordan and Horn<sup>7b</sup> recently collected 6 cases from the literature and contributed 5 of their own. Additional cases of pharyngeal neurilemmoma have been reported by Turchik,<sup>3a</sup> Violé<sup>7a</sup> and others.<sup>11</sup>

There appears to be no common causative factor contributing to the genesis of these tumors, although some authors associate their occurrence with von Recklinghausen's disease. In about 18 per cent of cases, solitary neurilemmomas are found coexistent with frank or suspected multiple neurofibromatosis.<sup>12</sup> Pharyngeal neurilemmomas are encountered about equally in the two sexes between the ages of 20 and 65. In our experience they have all been found in women.

Pharyngeal neurilemmomas when small will remain asymptomatic over a period of many months. The most frequent presenting complaints are the awareness of a mass in the throat and some degree of dysphagia. A neurilemmoma arising from the perineurium of a sympathetic nerve or involving the postganglionic fibers of the superior cervical ganglion may result in a Horner syndrome. Usually this syndrome is encountered more commonly as a transient postoperative complication,<sup>13</sup> but it may persist for months.<sup>14</sup> Segmental cervical root pain is not uncommonly experienced in cases of cervical neurilemmoma but less frequently encountered when the pharynx is involved. Hoarseness and some degree of dysphagia are experienced when the vagus nerve, particularly the medial and external portion containing the special visceral efferent fibers, is involved. Weakness of the ipsilateral shoulder occurs when the expanding neoplasm encroaches on the spinal accessory nerve, disturbing the innervation of the trapezius muscle.<sup>8</sup> Dyspnea is a late sign observed in patients in whom the tumor has assumed large proportions. Ulceration and hemorrhage

10. New, G. B., and Childrey, J. H.: Tumors of the Tonsil and Pharynx (Three Hundred and Seventy-Five Cases): I. Benign Tumors (Sixty-Three Cases), *Arch. Otolaryng.* **14**:596 (Nov.) 1931.

11. Motely, F. E.: Position Malignancy, *Arch. Otolaryng.* **34**:771 (Oct.) 1941. Fantuzzi, L.: Retropharyngeal Neurinomas, *Oto-rino-laring. Ital.* **14**:134 (March-April) 1946. Michl, R.: Neurinoma of the Hypopharynx, *Lék. listy* **2**:168, 1947. New, G. B., and Devine, K. D.: Neurogenic Tumors of the Nose and Throat, *Arch. Otolaryng.* **46**:163 (Aug.) 1947. Hall and Owens.<sup>8b</sup> Cutler and Gross.<sup>3b</sup> Turchik.<sup>3c</sup> Bustos.<sup>3e</sup>

12. Stout, A. P.: Neurofibroma and Neurilemmoma, *Clin. Proc.* **5**:1, 1946.

13. Hill, F. T.: Neurofibroma of the Pharynx with Paralysis of the Larynx Following Operation, *Ann. Otol., Rhin. & Laryng.* **53**:326, 1944. Nigro.<sup>3c</sup>

14. Turchik.<sup>3a</sup> Violé.<sup>7a</sup>

generally do not occur. On physical examination a tumor mass may be found in the anterior cervical triangle or beneath the sternocleidomastoid muscle, but in any case a bulging of the pharyngeal wall is encountered, usually arising from the tonsillar fossa. The tumor has a slightly movable "rubbery feel" and if large may be cystic. The



Fig. 1.—*A*, Encapsulated neurilemmoma of the left vagus nerve (case 4). *B*, the sectioned surface is tan-gray and gelatinous. In the central portion hemorrhage, degeneration and liquefaction necrosis are present.

mucous membrane is unattached and may move freely over the neoplasm. The shadow cast in a roentgenogram is not characteristic and cannot be distinguished from the shadow cast by any other soft tissue tumor.

Neurilemmomas are usually solitary encapsulated tumors (fig. 1). The surface is smooth but may be irregularly lobulated. The sectioned surface is brown-gray, resembling the color of a cross section of

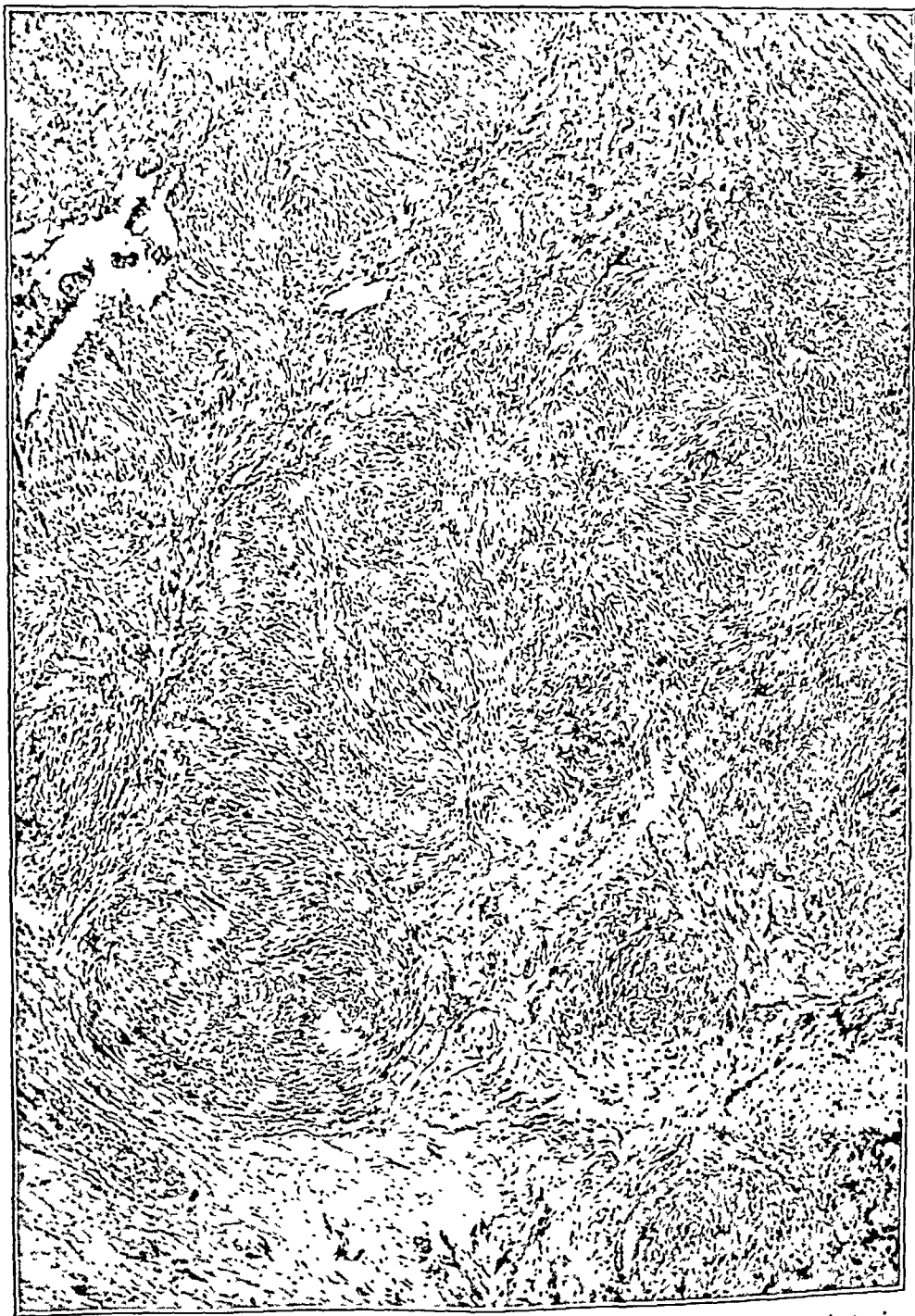


Fig. 2.—Photomicrograph of the tumor in case 3. Type A and B Antoni tissues are seen. "Verocay bodies" composed of palisading schwannian cells are present. Hematoxylin and eosin;  $\times 70$ .

nutmeg. In the central portion of the tumor, hemorrhage, degeneration and liquefaction necrosis are commonly found. The larger tumors are usually soft and cystic as a result of central necrosis. Central liquefaction necrosis is not observed in neurofibromas, even though the tumor may attain large dimensions.<sup>12</sup>

The histopathology is characteristic, consisting of two types of tissue (fig. 2). Antoni type A tissue is made up of a palisading long-fibered reticulum passing between elongated nuclei. This tissue is compact, in contrast to Antoni B tissue. Occasionally, "Verocay bodies" are found in the Antoni A component. These bodies are composed of highly differentiated schwannian cells with wiry reticulin fibers. Interspersed throughout the A tissue is the loosely textured Antoni B tissue, composed of schwannian syncytium without palisading. In this syncytium are microcysts produced by intracellular edema. These may coalesce and form visible cystic spaces. Hemorrhage and necrosis are found throughout the central portion of the larger neurilemmomas.

The schwannian theory of histogenesis has been strongly favored on the basis of the results of tissue culture studies of Murray, Stout and Bradley.<sup>3d</sup> The cells of these specific nerve tumors are morphologically and physiologically similar to the cells of Schwann.<sup>9</sup>

#### REPORT OF CASES

CASE 1.—*History*.—E. L. R., a white woman, 65 years of age, was admitted to the hospital complaining of progressive dysphagia, "throbbing" in the throat and dyspnea on lying down, of four years' duration. A slowly growing pharyngeal tumor mass was the cause of her symptoms. An unsuccessful attempt at removal through a lateral cervical incision had been made elsewhere seven months previously. Subsequently she was hospitalized at another institution, where she was considered to have an arteriovenous aneurysm, or "pulsating hemangioma," of the left posterolateral pharyngeal wall. Five radon seeds had been inserted into the tumor.

*Examination*.—The essential physical findings were the presence of a smooth, bulging tumor mass, firm but not hard in consistency, oval in shape, occupying the left posterolateral portion of the pharynx. The lesion extended superiorly from the vault of the nasopharynx down to the level of the cricoid cartilage. It extended from the median raphe to the anterior tonsillar pillar and occupied half the lumen of the pharynx. The covering mucosa moved freely over the tumor and was infiltrated with numerous small bluish veins. The entire mass seemed to pulsate, but critical examination showed this to be transmitted pulsation from a single large arterial trunk which curved about the medial border of the tumor, mainly in the midline.

Needle exploration of the tumor after local infiltration with procaine hydrochloride proved it to be solid. An aspiration biopsy was done, and the slides were interpreted as schwannoma (by Dr. Frank W. Foote, of New York).

Neurologic examination revealed no abnormalities, and both vocal cords had normal motility. The patient's blood pressure was 230 systolic and 130 diastolic, and there was hypertensive and arteriosclerotic retinopathy.

The patient was obviously a poor operative risk, but excision of the tumor was elected because of the severe and progressive dysphagia and dyspnea.

*Operation.*—With the patient under intratracheal anesthesia, the left external carotid artery was ligated in continuity through a lateral cervical incision, no exploration being done other than identification of the vessel. Through a transoral approach, the left lateral pharyngeal mucosa was incised from above downward, just posterior to the tonsil, after retraction of the soft palate. Mucosal flaps were developed, and an oval encapsulated tumor mass was exposed. It was in intimate contact with a large arterial trunk coursing over its medial surface. This was retracted to the right, and the tumor was freed by blunt and sharp dissection. As the operation progressed, it became evident that the artery medial to the tumor was the internal carotid. Because of a hesitant spirit, and adhesions following previous operation and irradiation, the tumor was removed in pieces rather than by dissection of the intact capsule. The most inferior fragment of the tumor was found to blend into a nerve trunk, which obviously was the vagus. The internal carotid pulsated freely after removal of the tumor mass.

*Postoperative Course.*—As the patient reacted from the anesthesia, it was apparent that she had a right hemiplegia. She slowly recovered over a period of twenty days, and paralysis of the left vocal cord was found after speech was resumed. It is our belief that the left cerebral ischemia was due to retraction compression of the left internal carotid artery during the operation and that the left recurrent laryngeal nerve fibers were interrupted by crude dissection of the tumor from the left vagus nerve.

*Pathology.*—The resected tumor tissue showed the typical microscopic picture of a neurilemmoma of the Antoni type A pattern, with palisading and "Verocay bodies."

*CASE 2.—History.*—B. D., a 68 year old white woman, was admitted to the hospital on Jan. 31, 1946, with complaints of pain in the left tonsillar and occipital area and dysphagia of three months' duration.

*Examination.*—A large smooth, bulging tumor mass was present in the area of the left tonsil, soft palate and lateral portion of the pharynx, extending into the pterygoid space. It encroached on the airway and was palpable in the neck behind and below the angle of the mandible. The overlying mucosa was not implicated and was movable over the tumor. The mass was firm and slightly movable, and a large pulsating artery was present in the medial and posterior aspect of the mass. The aspiration biopsy was reported as showing a picture consistent with the diagnosis of neurilemmoma. External ocular signs and the larynx were normal.

*Operation.*—With the patient under intratracheal cyclopropane anesthesia, a curved incision was made from the mastoid process below the mandible to the mental region. The bifurcation of the carotid artery was exposed, and the encapsulated tumor mass was found presenting medially and pushing the artery forward. The external carotid, occipital, external maxillary and temporal arteries were ligated and divided to expose the mass. The internal carotid artery was found to be deep and pushed to the midline of the pharynx by the tumor mass. The tumor mass did not arise in the bifurcation of the carotid artery and was not attached to the artery.

The vagus nerve was found spread out over the tumor, and by blunt dissection the mass was enucleated from the lateral pharyngeal space. It was found to extend from the base of the skull down to the left of the bifurcation and was enucleated

without breaking the capsule. It was attached to the hypoglossal nerve and apparently arose from it. This nerve was sectioned and resutured. The wound was closed with interrupted sutures and drains.

*Postoperative Course.*—The hospital course was uneventful. The patient was discharged on the sixth postoperative day, with paralysis of the left recurrent nerve and some dysphagia which persisted for three months, after which full recovery was noted. External ocular signs remained normal.

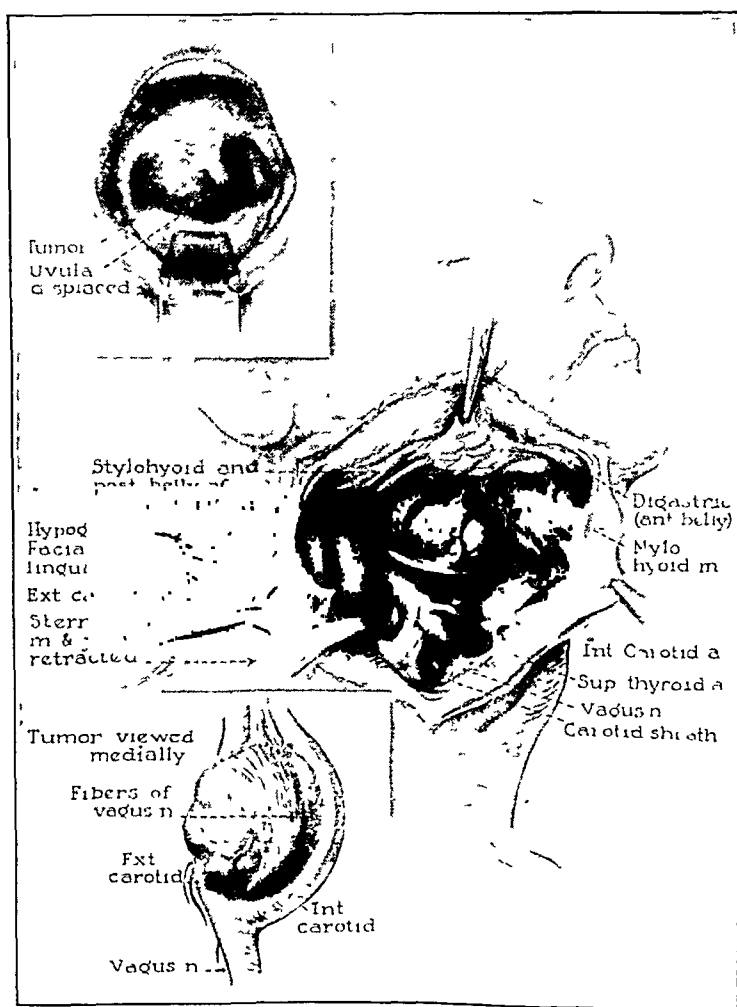


Fig. 3.—Composite and diagrammatic reconstruction of appearance of tumor when exposed through external cervical approach. Upper insert: intraoral view showing bulging tumor mass; lower insert: relationship of vagus nerve to tumor.

*Pathologic Examination.*—"The specimen consisted of a well encapsulated tumor. On palpation a few nodules were felt. The mass measured 5 by 4 by 2.5 cm. On sectioning, the capsule was gray, measuring 0.1 to 0.2 cm. in thickness. The tumor grossly appeared lobulated, separated by relatively firm gray tissue. A few foci of necrosis were noted as well as areas of hemorrhages. There were yellow areas scattered all over the specimen.



Microscopic examination showed that the tumor was characterized by varied areas; there were cellular fibrillar zones with more or less interwoven bands in areas, combined with palisading. In addition, there were extensive areas of marked edema, other areas of dense fibrosis and, again, areas of frank necrosis. The tumor was highly vascular, and many of the blood vessels were surrounded by hyalinized zones, often containing many fat-laden monocytes. There were also scattered hemosiderin-laden monocytes and scattered areas of round cell infiltration. The tumor was, in all, fairly well confined and revealed no microscopic evidence of frank malignancy. The diagnosis was neurilemmoma.

*CASE 3.—History.*—M. F., a 60 year old Negro housewife, was admitted to the hospital on Aug. 6, 1947, complaining of a mass in her throat with progressive difficulty in swallowing of four years' duration. For the last month there had been obstruction of the airway, and she was admitted to the surgical service on a semi-emergency basis because of stridor and the imminent necessity of tracheotomy.

*Examination.*—There was a smooth, lemon-sized mass protruding from the right tonsillar fossa, occupying half the pharyngeal space and extending deeply into the hypopharynx. The overlying mucosa was movable and not infiltrated by the tumor. On the posteromedial aspect of the tumor, almost in the midline of the pharynx, a pulsating large artery was present. Direct laryngoscopy revealed flaccid paralysis of the right vocal cord.

*Operation* (fig. 3).—With the patient under intratracheal anesthesia, a Bastia nelli type of incision was made on the right. The sternomastoid muscle and jugular vein were located and retracted posterolaterally, and the underlying tumor mass was exposed. There was marked distortion of the carotid vessels, the external carotid artery with its branches coursing over the external surface of the mass and the internal carotid artery being displaced medially at a sharp angulation. The lower pole of the tumor blended into the vagus nerve, and the mass extended up behind the mandible into the pterygoid space. The stylohyoid muscle and the posterior belly of the digastricus were divided, and the external carotid and interfering branches were ligated and sectioned. The tumor was dissected free rather easily with its capsule intact, without a break in the pharyngeal mucosa and without complete section of the vagus nerve. The nerve fibers were spread over the tumor and could be separated without difficulty.

*Postoperative Course.*—Recovery was uneventful, and the patient was discharged five days after operation. There was full recovery of her voice. On indirect examination, the larynx was normal. The patient was last seen on July 9, 1948, one year after operation. Her only complaint was occasional lancinating pain in the right mandible and parotid area on eating.

*Pathology.*—"The specimen consisted of an encapsulated, soft, ovoid mass with a pink-tan, shiny, smooth surface. It measured 7 by 3 by 2.5 cm. and had been previously opened. The cut surface was soft, and heterogenous white, red, brown, yellow-tan and glassy mucoid areas were also seen. On microscopic examination, the section revealed an encapsulated tumor mass composed of rather vascular fibrous tissue in a loosely whorled arrangement with many areas of hemorrhage, degeneration and necrosis. The nuclei were pleomorphic and oval shaped, with a tendency toward palisading and giant cell formation." The diagnosis was neurilemmoma.

*CASE 4.—History.*—P. M. A., a 53 year old white factory worker, was admitted to the hospital on Nov. 7, 1948, complaining of a "neck tumor" accompanied with hoarseness, dysphagia and pain radiating over the left side of the neck, face and

head. Symptoms had been present for seven years. At another institution, the tumor had been incised and drained twice, yielding "dark green water" and temporarily relieving the patient's symptoms. A tonsillectomy four years prior to her admission did not affect the tumor or alleviate her symptoms. The patient was told that a "ruptured pulsating blood vessel" over the tumor prevented transoral removal.

*Examination.*—There was an indurated scar beneath the angle of the left mandible. A lemon-sized rather soft tumor mass was found arising from the left tonsillar fossa and extending across to the midline of the pharynx and deep into the hypopharynx. A pulsating vessel lay over the medial border of the tumor beneath the mucosa of the pharynx. The pharyngeal mucosa was hyperemic but freely movable over the tumor. The larynx was edematous and injected. The left vocal cord was paretic. Conditions observed on ocular examination were within normal limits.

*Operation.*—With the patient under intratracheal thiopental sodium (pentothal sodium®)—ethylene anesthesia, a modified Bastianelli incision was made. The sternocleidomastoid muscle and internal jugular vein were retracted posterolaterally to expose the tumor. The external carotid artery and branches were displaced anteriorly by the tumor, while the internal carotid was displaced to the midline. The tumor arose from the vagus nerve (left) and extended from about the level of the larynx into the pterygoid space to the base of the skull. After division of the stylohyoid muscle and the posterior belly of the digastric muscle, the tumor was extirpated by sharp and blunt dissection. The tumor with its capsule was removed intact without damaging the pharyngeal mucosa. The vagus was not divided but was dissected from the tumor capsule with little difficulty. A transient bradycardia attended the extirpation of the tumor. A rapid recovery of normal cardiac rate occurred after the tumor was removed. The wound was closed with interrupted cotton sutures and drained.

*Postoperative Course.*—A transient Horner syndrome (left) persisted for forty-eight hours after operation. The patient was discharged on the eighth postoperative day without relief of her hoarseness but with relief of the dysphagia and some of her painful symptoms.

*Pathology.*—"The specimen consisted of an ovoid tumor which measured 5 by 3.5 by 1.5 cm. (fig. 1). It felt cystic and moderately soft. The surface was covered by a thin capsule. Attached to one portion was a fibrillar structure resembling nerve fiber. The sectioned surface was tan-pink and somewhat gelatinous. In the central portion there were cystic degeneration, hemorrhage and necrosis. Microscopic examination revealed that the tissue was made up of fibroblastic cells arranged in many areas in palisades. There was considerable diversity in the appearance of the various cells. Occasional mitotic figures were observed. In other areas there were hemorrhage and hemosiderin-filled macrophages. A section of nerve tissue was found associated with the fibrous capsule." The diagnosis was neurilemmoma.

#### COMMENT

These 4 cases have several points in common: The tumors were of relatively slow growth; they produced serious symptoms which would have led to a fatal termination if unrelieved; all 4 were benign, and all were surgically remediable. In 2 of the cases the diagnosis was made by aspiration biopsy. These 4 cases present certain clinical

features which, taken together, should allow a presumptive diagnosis of neurilemmoma of cranial nerve origin. These features are: the presence of a submucosal tumor mass protruding into the postero-lateral pharyngeal area; the history of slow growth; the presence of a single large pulsating arterial trunk at the medial limits of the tumor, and evidence of paresis of the vagus, hypoglossal or accessory nerves. The last feature is inconstant, but when it is present with the other features it should fairly clinch the diagnosis. In 2 of our patients interference with a cranial nerve was evident before operation—in these instances the vagus. This feature also has been noted by Turchik.<sup>15</sup> Medial displacement of the internal carotid artery has been mentioned once as an incidental observation in a case of tumor of the upper portion of the vagus nerve, but in this report pharyngeal symptoms or changes were not described.<sup>16</sup> Violé<sup>7a</sup> has noted a tendency of the tumor to force the artery outward when the neoplasm was found anterior to the carotid sheath and below the upper third of the sternocleidomastoid muscle.

The tumors which could be most commonly confused with a neurilemmoma of cranial nerve origin are, in order of importance, mixed tumors of salivary gland type arising in mucous glands of the pharyngeal or palatal mucosa, adenocarcinoma of the same origin, lymphosarcoma and "lymphoepitheliomas" of the tonsil without mucosal ulceration, chordomas and tumors of the carotid body. All these tumors should be readily differentiated by aspiration biopsy if an actual smear of tumor tissue is obtained. The microscopic patterns of these lesions are fairly distinct, even on smear. The aspiration biopsy technic<sup>15</sup> should be useful at least in differentiating benign and malignant tumors. On anatomic grounds, none of the tumors mentioned could displace the internal carotid artery medially, except a carotid body tumor, as mentioned in 1 instance by Lahey.<sup>16</sup>

Treatment of pharyngeal neurilemmomas of cranial nerve origin is entirely surgical. Irradiation is not only useless but harmful. It is our opinion that the lateral cervical approach is far better than a transoral one. The principal hazard in excision is hemorrhage, and this can be prevented or controlled much more easily by a wide exposure, identification and retraction of vulnerable vessels and their dissection under direct vision. The pharyngeal mucosa can be dissected free without penetration, permitting the operative procedure to be done without contamination, a maneuver impossible to achieve

15. Martin, H. A., and Ellis, E. B.: Aspiration Biopsy, *Surg., Gynec. & Obst.* **59**:578, 1934.

16. Lahey, F. H., and Warren, K. W.: Tumors of the Carotid Body, *Surg., Gynec. & Obst.* **85**:251, 1947.

by the transoral route. Actually the dissection of these tumors by the external approach is easier than might be imagined because of the displacement of important structures by the tumor.

A neurilemmoma may occasionally show malignant tendencies, metastasizing<sup>3b</sup> and revealing a microscopic picture with abnormal giant cells and mitoses.<sup>17</sup> Furrer and Fox<sup>18</sup> have published a case of perineural fibrosarcoma of the left vagus sheath metastatic to the tail of the pancreas. The presenting clinical findings were progressive hoarseness and dysphagia and on the left cervical pain and Horner's syndrome. Evidence of a cervical tumor was not conclusively established until the last few months of the patient's illness.

Neurilemmomas if completely excised do not locally recur. Pharyngeal neurilemmomas, potentially malignant, destroy locally by expansion and pressure necrosis. For these reasons they should be extirpated.

#### SUMMARY

The clinical findings and surgical management of 4 patients with neurilemmomas originating in the upper cervical cranial nerves are described. Three of these tumors arose from the vagus nerve and 1 from the hypoglossal.

Certain features common to all 4 cases would seem to allow a clinical diagnosis of such lesions. These are: (1) a bulging, firm submucosal tumor mass presenting in the posterolateral pharyngeal wall, causing dysphagia and, later, interference with the airway; (2) pulsation of the tumor mass, due to medial displacement of the internal carotid artery, and (3) interference with function of the nerve involved. Two of the patients with tumors of the vagus nerve had paralysis of the vocal cord on the same side.

Extirpation of these lesions is best done through an external cervical approach.

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17. Foot, N. C.: *Pathology in Surgery*, Philadelphia, J. B. Lippincott Company, 1935, pp. 438-441.

18. Furrer, E. D., and Fox, F. R.: *Perineural Fibrosarcoma of the Left Vagus Sheath: Report of a Case*, *West. J. Surg.* **48**:584, 1940.

## TREATMENT OF THE "SHOCK KIDNEY"

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DETROIT

**S**HOCK may be defined as a condition of acute prolonged depression of blood pressure and circulating blood volume. Among the conditions in which it occurs are anaphylaxis, coronary occlusion, poisonings of various kinds, overwhelming infections and, most important from our standpoint, trauma and hemorrhage.<sup>1</sup>

This is not the place to discuss the various theories of the mechanism of traumatic shock, or to attempt to detail or analyze the great confusing mass of experimental and clinical observations which continue to appear in the literature. It is enough to say that there are three theories of the underlying mechanism of traumatic shock: first, that it is of predominantly nervous origin; second, that there is produced by trauma a circulating vasodepressor substance, and, third, that it is due to loss of blood, either externally or internally into the tissues. At present, the consensus is that though the nervous system and a circulating depressor substance may be factors, the primary cause in practically all cases of traumatic shock is hemorrhage.<sup>2</sup>

The "shock kidney" is the renal condition which may accompany or follow prolonged, profound circulatory depression; it is characterized by oliguria or anuria, increasing azotemia, and, usually, the presence of heme casts in whatever urine may be excreted.<sup>3</sup>

The clinical aspects have long been known, and the pathologic features have been described in the past, but it has been only in the last decade that confusion has been dispelled and the clinical and

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1. Moon, V. H.: *Shock: Its Dynamics, Occurrence, and Management*, Philadelphia, Lea & Febiger, 1942.

2. (a) Freeman, N. E.: *Newer Concepts of the Pathologic Physiology of Shock*, *S. Clin. North America* **26**:1319, 1946. (b) Gregersen, M. I., and Root, W. S.: *Experimental Traumatic Shock Produced by Muscle Contusion with a Note on the Effects of Bullet Wounds*, *Am. J. Physiol.* **148**:98, 1947. (c) Moon, V. H.: *The Pathology of Secondary Shock*, *Am. J. Path.* **24**:235, 1948. (d) Swindler, C. M.: *Hemorrhagic Shock*, *Am. J. Surg.* **76**:182, 1948.

3. Moon, V. H.: *Renal Deficiency Associated with Shock*, *J. A. M. A.* **134**:425 (May 31) 1947.

pathologic features coordinated into a clear, though still somewhat provisional, picture on which a rational plan of treatment can be based.

The clinical observations and pathologic studies made by Byswater, Mallory,<sup>4</sup> Lucke<sup>5</sup> and others during and after the war on persons dying after battle injuries or from crush injuries, supplemented by experimental and clinical observations by Trueta,<sup>6</sup> Corcoran and Page,<sup>7</sup> Thorn, Van Slyke<sup>8</sup> and others, have brought about the present conception.

To this renal condition Lucke, has given the name "lower nephron nephrosis," which has been widely adopted. Like all labels, it can be used as a substitute for thinking, and undoubtedly in individual cases important conditions of the kidney have been masked by the mere application of this label. Synonyms are prerenal azotemia, hepatorenal syndrome and hemoglobinuric nephrosis.

The condition is not peculiar to shock, and, in fact, is seen more frequently in other circumstances. Among the commoner exciting causes are intravascular hemolysis associated with transfusion reactions; heatstroke; uteroplacental damage; after abortion; sulfonamide sensitivity, and from various poisons, notably carbon tetrachloride.<sup>2c</sup>

It is probably never seen completely uncomplicated by lesions in other organs, but the complications are much less in evidence in some of the cases of the mild toxic form, such as those associated with pregnancy, intravascular hemolysis and sulfonamide sensitivity, than in the cases associated with traumatic shock. Even in the cases of the mild toxic condition, however, some hepatic damage is undoubtedly present, and in cases of shock there is reason to believe that a biochemical lesion of the liver is responsible for the rapid deterioration of the shock state, for damage to the kidney and adrenal gland is not immediately important, since loss of function there is not so rapidly lethal.<sup>9</sup>

Typically the affected kidney has the following gross characteristics: It is large, smooth and pale; on cutting, the cortex is pale and the

4. Mallory, T. B.: Hemoglobinuric Nephrosis in Traumatic Shock, *Am. J. Clin. Path.* **17**:427, 1947.

5. Lucke, B.: Lower Nephron Nephrosis, *Mil. Surgeon* **99**:371, 1946.

6. Trueta, J.; Barclay, A. E.; Daniel, P. M.; Franklin, K. J., and Prichard, M. M. L.: *Studies of the Renal Circulation*, Springfield, Ill., Charles C Thomas, Publisher, 1947.

7. Corcoran, A. C., and Page, I. H.: Crush Syndrome: Post-Traumatic Anuria, *J. A. M. A.* **134**:436 (May 31) 1947.

8. Van Slyke, D. D.: The Effects of Shock on the Kidney, *Ann. Int. Med.* **28**:701, 1948.

9. Fine, J.; Seligman, A. M., and Frank, H. A.: On the Specific Role of the Liver in Hemorrhagic Shock, *Ann. Surg.* **126**:1002, 1947. Shorr, E.: Hepato-Renal Factors in Traumatic and Hemorrhagic Shock, *Bull. Johns Hopkins Hosp.* **81**:70, 1947.

medulla is congested and has prominent striations. Microscopically the glomeruli appear essentially normal, the chief lesion being necrosis of the cells of the distal convoluted tubules and the ascending or thick limb of the loop of Henle, with heme casts in the tubules (fig. 1).

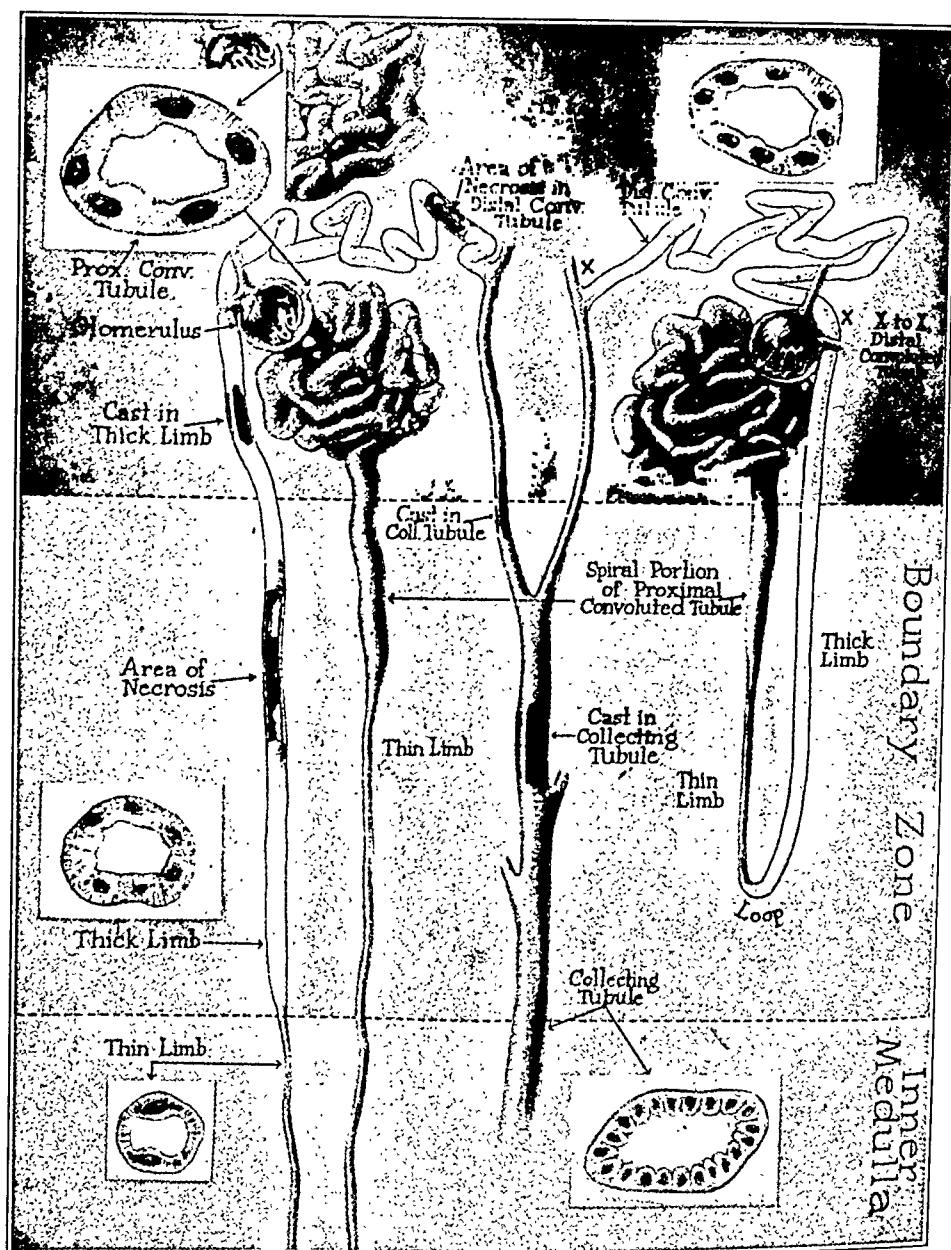


Fig. 1.—Structure of the normal nephron and site of the lesion in lower nephron nephrosis. (From Lucke.<sup>5</sup>)

This is a simplified or typical picture. Of course it may be engrafted on any previously existing renal disease, and it is probable that further progress of the agent or condition producing it may cause more exten-

sive lesions involving the proximal portions of the nephron even including the glomerulus.

Theoretically in shock these lesions are brought about by anoxia. As a matter of fact, the early effects of toxins and of anoxia on the liver and kidney cells are indistinguishable and there is good reason to believe that toxic substances act on these cells by inciting anoxia, and the longer the anoxia persists the more extensive should be the injury.

The kidney apparently ranks with the liver in the ability to withstand anoxia—not so vulnerable as the brain but more so than skeletal tissues. Therefore there should be a stage in which if the anoxia is ended no damage to the kidneys would be observed, and clinically this is the case. In other words, the damage is a function of the time of action of the cause. Mallory<sup>4</sup> concluded that the successive stages of the lesions were as follows: (1) within twenty-four hours lipid vacuolation of the cells of the ascending limb of the loop of Henle; (2) twenty-four to seventy-two hours after injury precipitation of heme casts in distal tubules and (3) occasionally on the third and regularly on the fourth and fifth days, necrosis and regeneration of the epithelium of the ascending limb and distal tubules. When the damage is at its height, the tubules lose their ability of selective resorption and any filtrate received by them from the glomeruli is poured back into the blood stream.

Before the present conception of the course of events, the thinking regarding the process going on in the kidney and the proper way to handle it was rather foggy. There was a vague idea that the glomeruli required stimulation and that the tubules were blocked by the heme casts; so the accepted treatment was the attempt to simulate the glomeruli and wash out the plugging casts by the pouring in of vast quantities of fluid—with the common result, since fluid was not being eliminated by the kidneys, that the circulation became overloaded and insufficient, and death too often occurred with pulmonary edema. This is not to say that this circulatory embarrassment was the invariable or sole cause of death. In many cases extensive hepatic damage was found to be present. Experience has shown that the renal lesions are reversable and that if the toxin or other deleterious substance is eliminated, normal circulation restored and the life of the patient preserved long enough, the tubular cells will regenerate and reassume their normal function. Mallory observed regeneration as early as the fourth day after injury.

Oliguria and anuria are spectacular, attention-arresting, phenomena and in the past have held too alarming a place in the mind of the



surgeon. Moreover, the dangers of azotemia have been exaggerated. On record are the patients who have lived more than three weeks after a solitary kidney was removed and in everybody's experience is the patient with chronic renal disease, polycystic or otherwise, who lives an active life for months in spite of azotemia.

Particularly in the early stages, the danger of anuria or oliguria is not that of poisoning by the products of metabolism but of retention of fluids and imbalance of electrolytes and carbon dioxide.

The treatment of shock kidney can be considered under four heads: prevention; maintenance of fluid balance; maintenance of electrolyte balance, and treatment of azotemia.

1. *Prevention.*—Prevention of shock kidney consists in averting the loss of blood volume and pressure by the giving of blood and fluids before it takes place, or in restoring volume and pressure by the same means as soon as possible after it takes place. This must be done with discretion. Often the vascular system has been treated as if it resembled a somewhat leaky rigid vessel, and the attempt has been made to fill it to a certain mark—namely, normal blood pressure. It may be that a more useful comparison would be with a distensible vessel like the bladder, the overstretching of which may cause paralysis. So in the attempt to prevent or remedy shock probably not much more fluid (blood, plasma, etc.) should be given than will replace estimated blood volume loss. It is difficult to estimate the amount of blood loss and to determine the rate and the amount of transfusion under emergency conditions. Undoubtedly more patients have been saved by transfusions than have been drowned by too much blood, but the following 2 cases are suggestive.

CASE 1.—A man of 53, during operation for carcinoma of the cecum, received 1,000 cc. of blood, the blood pressure remaining stable throughout. After operation the urinary output per day, except on one day, did not exceed 325 cc., and it was calculated that the patient received an average of about 200 cc. of fluid per day above his total output. His nonprotein nitrogen level rose steadily till his death, on the thirteenth postoperative day. On the tenth day his blood pressure rose and signs of pulmonary edema appeared. Postmortem examination showed the lesions of lower nephron nephrosis superimposed on nephrosclerosis and early pyelonephritis. There was severe pulmonary edema and no hepatic damage.

CASE 2.—A 52 year old man was admitted with traumatic rupture of the left kidney, rupture of the spleen and fracture of two ribs. His condition improved with blood transfusions, and twenty-four hours after admission the left kidney and the spleen were removed. During operation he received 1,500 cc. of blood and his blood pressure remained on a satisfactory level. Shortly thereafter it fell so low as to be unobservable, and in the course of three hours he received an additional 2,500 cc. of blood. His blood pressure rose above the level it had held during operation, signs of pulmonary edema appeared, and he died two hours later. Autopsy showed only pulmonary edema and no fresh hemorrhage.

2. *Maintenance of Fluid Balance.*—In the presence of continued oliguria or anuria, only the amounts of fluid lost through perspiration, respiration and vomiting and through the bowels should be replaced. If no vomiting, diarrhea or profuse sweating occurs, the insensible loss is somewhere around 1,200 cc. a day.

Oliguria occurs commonly after operation, either on a nervous basis or owing to temporary lowering of the blood pressure (Trueta's description of a "shunt" of blood around the glomeruli is interesting in this connection). Such oliguria does not necessarily indicate renal damage, as is illustrated by the following case.

CASE 3.—A 52 year old man underwent a two stage thoracolumbar sympathectomy for hypertension. Before operation his blood pressure was 250 systolic, and 110 diastolic. After the first stage it was 200 systolic and 110 diastolic. During the second stage the blood pressure fell to imperceptible levels but was restored by the use of vasoconstrictors and the giving of blood and fluids. After operation it fell to 80 systolic and 40 diastolic, and there was associated oliguria with a nonprotein nitrogen content of 62 mg. per hundred cubic centimeters. In the next four days the blood pressure gradually rose to 150 systolic and 90 diastolic, the urinary output increased from 200 cc. to 1,550 cc. and the nonprotein nitrogen fell from 62 to 37 mg. per hundred cubic centimeters.

However, if oliguria persists, it means renal damage. The time at which such damage can be assumed is indefinite, though Mallory<sup>4</sup> stated that it is less than one day. The following case illustrates the rapidity with which the typical renal lesions may develop.

CASE 4.—A man of 45 underwent a difficult and lengthy operation for recurrent islet carcinoma of the pancreas. The blood pressure fell sharply during operation. Oliguria and rapidly increasing azotemia were observed during the three days he lived. Autopsy showed the typical lesions of advanced lower nephron nephrosis as well as acute parenchymatous degeneration of the liver and pulmonary edema.

3. *Maintenance of Electrolyte Balance.*—The sodium chloride content and carbon dioxide-combining power of the blood should be watched. Chlorides and sodium are not difficult to regulate by means of intravenous infusion or by diet. Acidosis is more difficult to remedy and in some cases yields to none of the usual methods of control.

Very appreciable amounts of salt are removed in the perspiration and by the urine after diuresis starts, but, in our experience, with the toxic lower nephron nephrosis no extraordinary measures have been necessary. There have been some observations on potassium levels, but their importance has not been determined.

4. *Treatment of Azotemia.*—Moderate levels of azotemia need cause no alarm. Even though deaths have occurred in association with azotemia levels of less than 100 mg. of nonprotein nitrogen per hundred cubic centimeters of blood, deaths in such cases have usually been due to other causes and severe hepatic damage was present in most. At what level azotemia begins to be dangerous is difficult to say. Cer-

tainly recovery has taken place after the nonprotein nitrogen level reached over 200 mg. per hundred cubic centimeters of blood, but probably some means of elimination are desirable before that figure is reached.

Sweating is an old and somewhat effective method for removing both fluid and nitrogen. It must be kept in mind that a good deal of salt is removed at the same time.

Many years ago Abel, Rountree and associates<sup>10</sup> and, more recently, Murray, Kolff and Alwall<sup>11</sup> have independently developed artificial kidneys and used the instruments in human patients. Efficient operation was made possible, first, by the production and purification of heparin so that the blood could be maintained in a liquid state outside the body and, second, by the development of suitable cellophane tubing through which dialysis could be accomplished. The underlying principles of all types are the same. A thin layer of heparinized blood is run through the cellophane tubing. Surrounding the tubing is the "rinsing" solution, which contains salts to approximate normal plasma—chlorides of sodium, potassium, calcium and magnesium; sodium hypophosphate and bicarbonate, and glucose. Through the dialyzing membrane pass diffusible materials from the blood which are in greater concentration than in the rinsing solution—most significantly the end products of nitrogen metabolism and other toxic materials usually excreted by the kidneys. The originators of the artificial kidney have reported spectacular instances in which it was used to tide patients over the critical period in cases of renal suppression until certain renal elements could regenerate and resume normal excretory function.

The apparatus is rather cumbersome and uncertain, however, and may cause hemorrhage or clotting. We have seen it used vainly in 2 of our cases, and it may have contributed to the fatal result in 1.

Favorable results have been reported with peritoneal perfusion.<sup>12</sup> In the literature are reports of about a hundred cases. We have never

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10. Abel, J. J.; Rountree, L. G., and Turner, B. B.: On the Removal of Diffusible Substances from the Circulating Blood of Living Animals by Dialysis, *J. Pharmacol. & Exper. Therap.* **5**:275, 1913-1914.

11. Alwall, N.: On the Artificial Kidney: I., *Acta med. Scandinav.* **128**:317, 1947; Clinical Extra-Corporeal Dialysis of Blood with Artificial Kidney, *Lancet* **1**:60, 1948. Kolff, W. J.: The Artificial Kidney, *J. Mt. Sinai Hosp.* **14**:71, 1947. Thalheimer, W.: Experimental Exchange Transfusions for Reducing Azotemia: Use of Artificial Kidney for This Purpose, *Proc. Soc. Exper. Biol. & Med.* **37**:641, 1937. Murray, G.; Delorme, E., and Thomas, N.: Development of an Artificial Kidney, *Arch. Surg.* **55**:505 (Nov.) 1947.

12. Frank, H. A.; Seligman, A. M., and Fine, J.: Treatment of Uremia After Acute Renal Failure by Peritoneal Irrigation, *J. A. M. A.* **130**:703 (March 16) 1946. Seligman, A. M.; Frank, H. A., and Fine, J.: Treatment of Experimental Uremia by Means of Peritoneal Irrigation, *J. Clin. Investigation* **25**:211, 1946.

used it after shock but have used it in 2 instances of azotemia, one being terminal nephritis. In both it seemed to function well and substantial amounts of nitrogen were found in the perfused fluids, and in both cases by its use the azotemia either diminished or was stabilized. It is simple to install. Our method was to introduce a Pezzar catheter into the peritoneal cavity high in the right flank for intake and a sump drain in the left lower quadrant for outlet. The chief drawback was

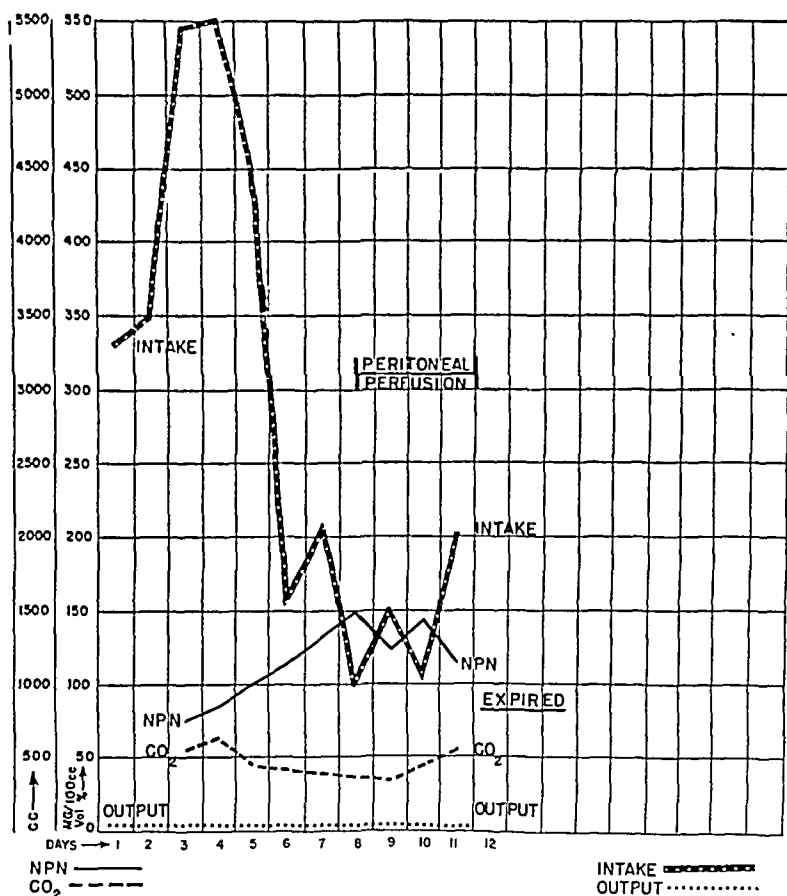


Fig. 2.—Chart from a fatal case of sulfadiazine poisoning, showing the effect of peritoneal perfusion on the nitrogen level. The apparatus was in operation between the fourth and twelfth days, during which the nonprotein nitrogen level of the blood fell, in spite of the fact that the urinary output remained stationary at a low level. On four occasions the nonprotein nitrogen level of the perfusing fluid varied between 64.5 and 131 mg. per hundred cubic centimeters. This patient received too much fluid in the early days of his treatment and died with pulmonary edema. There was also hepatic damage.

that it required the full time attention of someone—nurse or physician—to toy with the outlet tube to keep the fluid running, for the omentum has a tendency to wind itself about the outer tube of the drain. It

was interesting to see how by altering the constitution of the perfusing fluid alterations in blood chemistry could be brought about.

Acute peritonitis has been reported to follow use of this method. Both our patients died, and autopsy showed no acute peritonitis but did show opacity and thickening of the peritoneum, suggesting that the period of effectiveness of such perfusion might be limited. The accompanying charts show the effect on the blood and the amounts of nitrogen withdrawn (figs. 2 and 3).

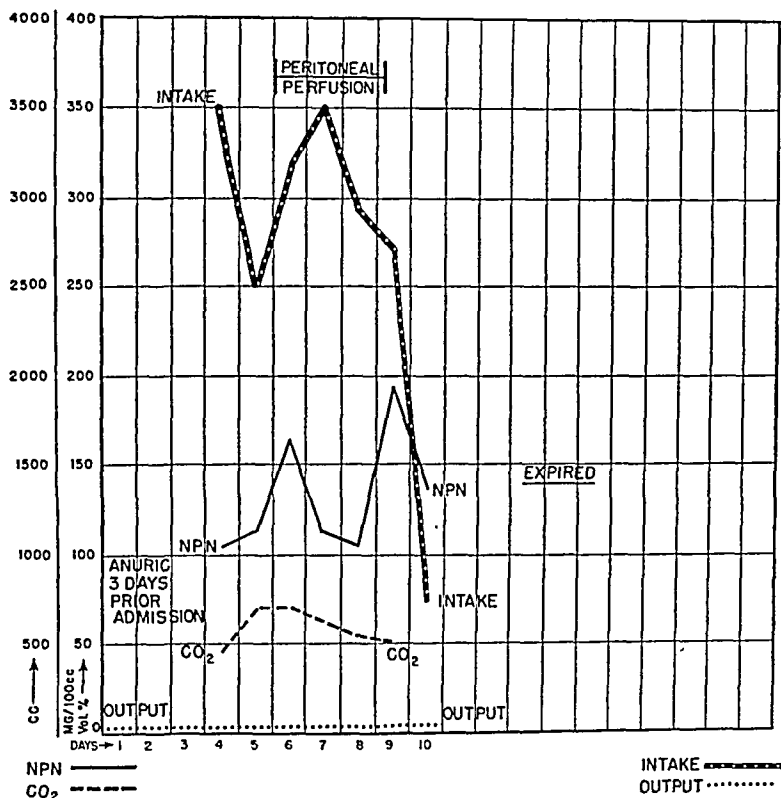


Fig. 3.—Effect of peritoneal perfusion on the nitrogen level in a terminal case of nephritis. During the application of peritoneal perfusion the nonprotein level of the nitrogen of the blood fell. On four occasions the nonprotein nitrogen level of the perfusing fluid varied between 68 and 115 mg. per hundred cubic centimeters.

In a few instances of azotemia we have used gastric and duodenal lavage and were favorably impressed.<sup>13</sup> We were able to diminish or stabilize the nonprotein concentration of the blood, and we could add or extract fluid or salt. Our rather small experience leads us to prefer this method to the others (fig. 4).

Other procedures which have been recommended in the treatment of certain types of anuria—renal decapsulation, spinal anesthesia and

13. Vermooten, V., and Hare, D. M.: The Use of Continuous Gastric Lavage in the Treatment of Uremia Associated with Prostatism, *J. Urol.* 59:907, 1948.

paravertebral block<sup>14</sup>—seem to have no place in the presence of, or following, shock. However, renal diathermy is certainly harmless and might well be tried.

The paradoxical conclusion that we reach, therefore, is that the treatment of the "shock kidney" consists in not treating the kidney. Treatment should be directed toward keeping the patient alive. If the patient lives long enough, regeneration of the renal cells will take place. In the over-all picture, the importance of the renal lesion consists in the fact that normal elimination is absent and the realization of this fact must be a controlling factor in the treatment of the patient.<sup>15</sup>

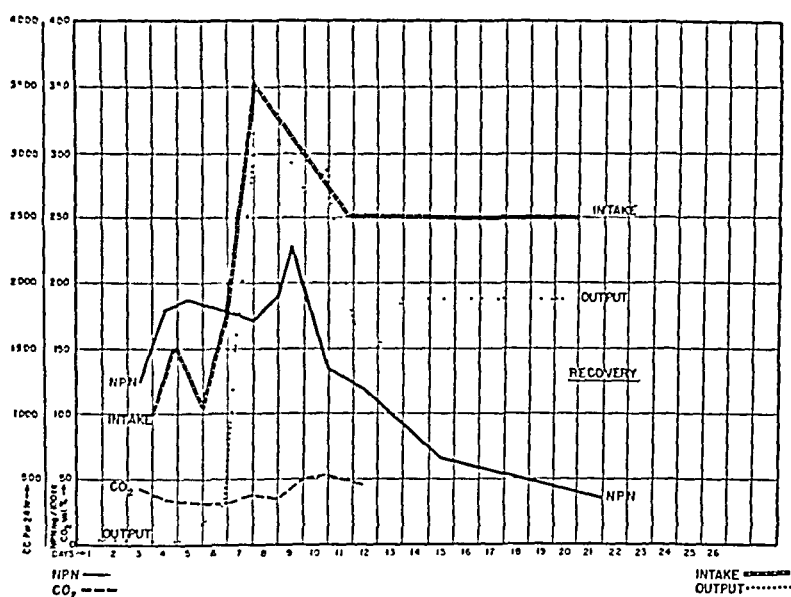


Fig. 4.—Chart of a patient with lower nephron nephrosis due to sulfadiazine poisoning. Gastric lavage was used between the fourth and seventh days, and the chart shows clearly that the nonprotein nitrogen level of the blood did not rise, though the urinary output remained low. On one of these days the gastric washings contained 66 mg. of nonprotein nitrogen per hundred cubic centimeters. On the seventh day the urinary output rose noticeably, and gastric lavage was discontinued; interestingly, the nonprotein nitrogen level rose for several days. This is a common observation in such cases after diuresis begins; the rise may be due to release into the blood of nitrogen which has accumulated in the tissues.

14. Trimble, I. R., and Sanford, M. C.: Relief of Renal Colic and Renal Suppression: A Preliminary Report, *J. Urol.* **55**:4, 1946. McGowan, J. M., and Autry, D. H.: Reflex Anuria: Its Treatment by Procaine Sympathetic Block, *Am. J. Surg.* **76**:205, 1948. Margraves, R. O., and Bogen, E.: Spinal Anesthesia in the Treatment of Reflex Anuria, *Urol. & Cutan. Rev.* **49**:279, 1945. Cubitt, A. W.: The Problem of Anuria, *Brit. J. Surg.* **24**:215, 1936.

15. Muirhead, E. E., and Hill, J. M.: The Treatment of Acute Renal Insufficiency, *Surg., Gynec. & Obst.* **87**:445, 1948. Strauss, M. B.: Acute Renal Insufficiency Due to Lower Nephron Syndrome, *New England J. Med.* **239**:693, 1948.

## CONCLUSIONS

1. Surgical shock is usually due to hemorrhage.
2. The lowered blood pressure of shock may cause damage to the kidney due to anoxia.
3. This damage is reversible if the patient can be kept alive long enough.
4. Treatment at first, therefore, is the treatment of shock—namely, restoration of normal blood pressure and effective blood volume.
5. Replacement of the estimated blood loss is preferable to the attempt to restore blood pressure by unlimited transfusions.
6. After the patient has recovered from shock, if the kidneys are not functioning only enough fluids and electrolytes should be given to replace the fluids and electrolytes lost.
7. If azotemia mounts to dangerous levels, some means of reducing it should be used. In our experience, gastric and duodenal lavage have proved satisfactory.

# TRANSPLANTATION OF THE SPINAL CORD FOR PARAPLEGIA SECONDARY TO POTT'S DISEASE OF THE SPINAL COLUMN

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THE PARAPLEGIA resulting from Pott's disease may occur in any stage of the disease and may be a result of several factors. Butler,<sup>1</sup> in a thoroughly studied series of cases, found the incidence of paraplegia in all stages of the disease to be 11.4 per cent. Other authors have cited figures of from 5 to 20 per cent as the incidence of paralysis in this disease. The results of treatment vary somewhat with the extent and neurologic type of the paralysis, the cause of the paralysis and the method of treatment.

It is evident that there are many pros and cons concerning the use of a surgical attack for the relief of paralysis due to tuberculous abscesses and granulation tissue, compression of the spinal cord by pathologic fractures of vertebral bodies, vascular and toxic disturbances of the spinal cord incident to tuberculous disease and the formation of bony ridges causing compression of the spinal cord. All these conditions may occur in connection with Pott's disease.<sup>2</sup>

Laminectomy for the relief of compression of the spinal cord is not without danger. The general health of the patients is not usually of the best. Laminectomy may mean a further weakening of an already weakened spinal column and the possibility of increasing the paralysis due to pathologic dislocations and of causing additional compression of the cord. It carries with it the risk of spreading the infection either locally or by a usually fatal tuberculous meningitis. In spite of these

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1. Butler, R. W.: Paraplegia in Pott's Disease, with Special Reference to the Pathology and Etiology, *Brit. J. Surg.* **22**:738-768 (April) 1935.

2. (a) Seddon, H. J.: Pott's Paraplegia: Prognosis and Treatment, *Brit. J. Surg.* **22**:769-799 (April) 1935. (b) Seddon, H. J., and Alexander, G. L.: Discussion on Spinal Caries with Paraplegia, *Proc. Roy. Soc. Med.* **39**:723-734 (Sept.) 1946. (c) Butler.<sup>1</sup>



considerations, it appears that a surgical attack has some place in the management of the paralysis occurring in this disease.

Paraplegia accounted for 50 per cent of the paralysis in one group of cases of Pott's disease which has been reported.<sup>2b</sup> This type of paralysis occurs late in the disease. Classically the patient has considerable deformity but has been getting along well after being treated for Pott's disease until he begins to experience some difficulty in walking. This may progress rather rapidly to a complete and total motor paralysis, from which recovery may be either slow or impossible. If recovery does take place, it occurs only after prolonged conservative treatment.

This late paraplegia has been considered to be due to the formation of a bony ridge and the further compression of the spinal cord or to interference with an already precarious blood supply to the adjacent cord. Butler recently stated that the paraplegia was due to the reactivation of the tuberculous process with the formation of granulation tissue and debris in the canal.

Inasmuch as there is interference with the conductivity of the cord regardless of the cause in this late stage, removal of the mass and decompression of the cord seem indicated as soon as paralysis becomes evident and especially if it progresses slowly.

Because of the marked angulation of the vertebral column found in this late stage, a procedure designed to free the cord of its compression and also to allow it to assume a more normal relationship seems to be preferable to a simple decompressive laminectomy. Hyndman<sup>3</sup> in 1947 described a technic for both anterior and lateral transplantations of the spinal cord in cases in which marked kyphosis or scoliosis existed. He reported 2 cases in which these procedures were used. It was his belief that in the majority of cases granulation tissue was the cause of the paralysis and that this procedure had no special application in the treatment of tuberculous kyphosis with signs referable to the cord. He also called attention to the use of anterior transplantation of the spinal cord for acute injuries followed by rapidly developing paralysis.

The possibility of offering patients with paraplegia secondary to bony compression of the spinal cord some chance of a reasonably useful life prompted the use of this procedure in 5 cases which are reported herein.

#### REPORT OF CASES

CASE 1.—The patient, a married man 28 years old, was seen at the Mayo Clinic on April 24, 1947, because of numbness and weakness in both legs. He gave the history of having fallen when 15 years old and striking the middle of his back. He ached for a few days, and then his symptoms vanished. Six months later he noticed sagging of his left shoulder. He was operated on at a hospital

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3. Hyndman, O. R.: Transplantation of the Spinal Cord: the Problem of Kyphoscoliosis with Cord Signs, *Surg., Gynec. & Obst.* **84**:460-464 (April) 1947.

in his locality (the procedure was unknown), and he was then in a body cast for one year. After the cast was removed, he noticed marked angulation of his back. He was advised to wear a brace for two years. He remained well until nine days prior to admission to the clinic, at which time he noticed spontaneous onset of weakness in both legs which progressed so that two days prior to registration he was unable to walk. Lumbar puncture elsewhere was unsuccessful. Nothing else of significance was noted in his medical or family history. He had been married for one year and was the father of a child.

Physical examination on admission showed marked kyphoscoliosis; the kyphosis was most pronounced in the lower part of the thoracic region. Neurologic examination showed a loss of sensation for pain and touch below the level of about the tenth thoracic segment (fig. 1) and a marked loss of motor power

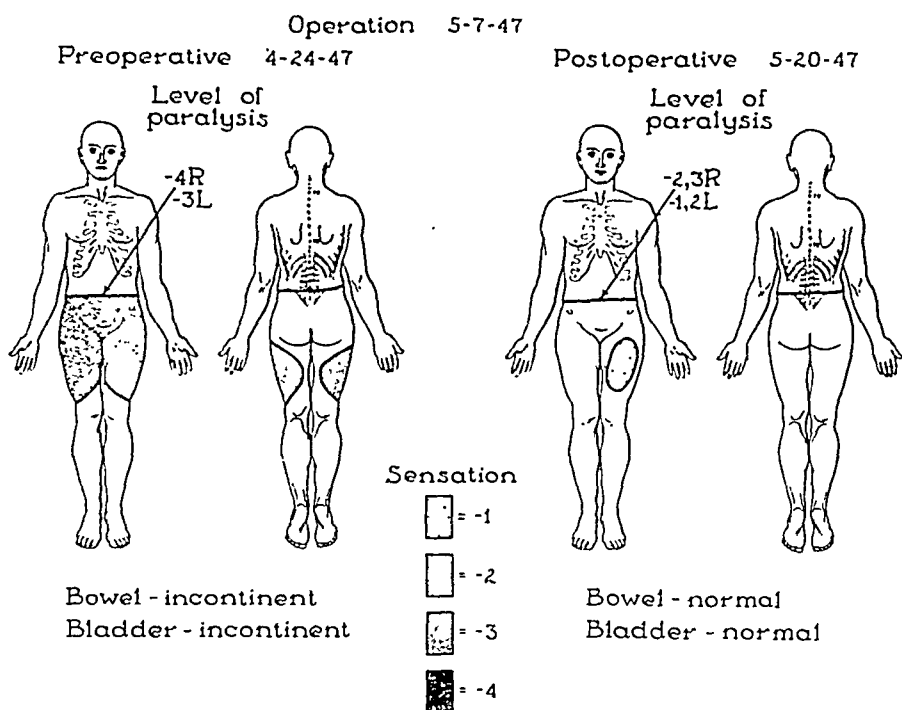


Fig. 1 (case 1).—The principal neurologic findings before operation and immediately after operation. The comparison of the drawings on the right with those on the left show the marked improvement which occurred after transplantation of the spinal cord.

below the first lumbar segment. Reflexes were noticeably increased in the lower extremities, and the patient had bilateral Babinski signs. He had some difficulty in voiding and defecating. An examination of the urine showed an occasional pus cell, but the concentration of hemoglobin, leukocyte count and results of flocculation tests were normal. Roentgenologic examination (fig. 2) revealed an extreme kyphoscoliosis of the thoracic portion of the spinal column, with the kyphosis most marked in the lower portion of the thoracic region. It was felt that the patient had an old Pott's disease of the thoracic portion of the spinal column.

He was hospitalized and placed in traction, but in five days his paraplegia had progressed so that he could no longer move his right foot and his bowels and bladder were completely uncontrollable.

On May 7, 1947, with the patient under general anesthesia, one of us (J. G. L.) performed an exploratory operation. The kyphos was explored from the fifth thoracic to the third lumbar vertebra. The bony portion of the kyphos was smooth and well fused, so that it was not possible to determine where one lamina began and another ended. When the apex of the kyphos was opened with a cranial burr, dense granulation tissue was encountered which covered the spinal cord. A large amount of pus and necrotic material also were found in this region.

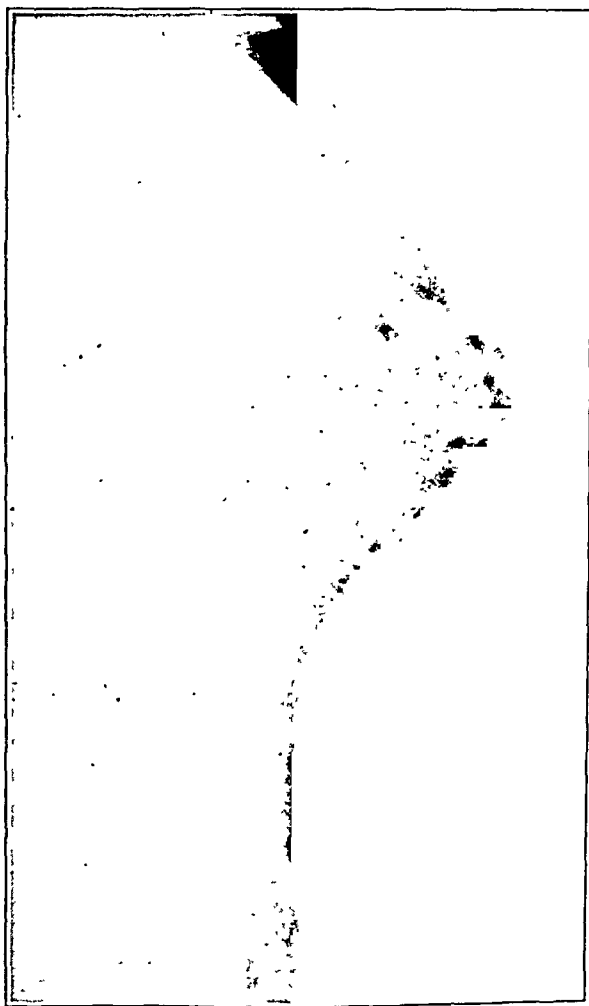


Fig. 2 (case 1).—The spinal column after operation showing the marked kyphosis and the silver clips placed on one of the divided nerve roots in the apex of the kyphos (lateral view).

The laminectomy was extended downward on each side of the apex of the kyphos to give exposure beyond the extent of the extradural granulation tissue. Several extradural abscesses were evacuated in the process. As the granulation tissue was removed, pulsations, which had not been evident before, could be seen in the spinal cord over the apex of the hump. The dura was not opened. Inasmuch as the cord still appeared to be tense in spite of the evacuation of much extradural debris, two nerve roots were divided on the left and one on the right (fig. 3).

This allowed mobilization of the spinal cord so that the bridge of bone anterior to the cord, which was producing the angulation, could be removed. Gelatin sponge soaked in thrombin was used to control the bloody oozing along the bony edges. The wound was then closed in layers without drainage.

The pathologic diagnosis of the removed tissue was tuberculous granulation tissue and caseous material.

For two days following the operation, the patient's temperature remained at 101 F., after which it became normal. He required catheterization for nine days after operation, and the sutures were removed on the ninth day.

Neurologic examination fourteen days after operation (fig. 1) showed sensation to be almost intact with some improvement in the right leg and definite improve-

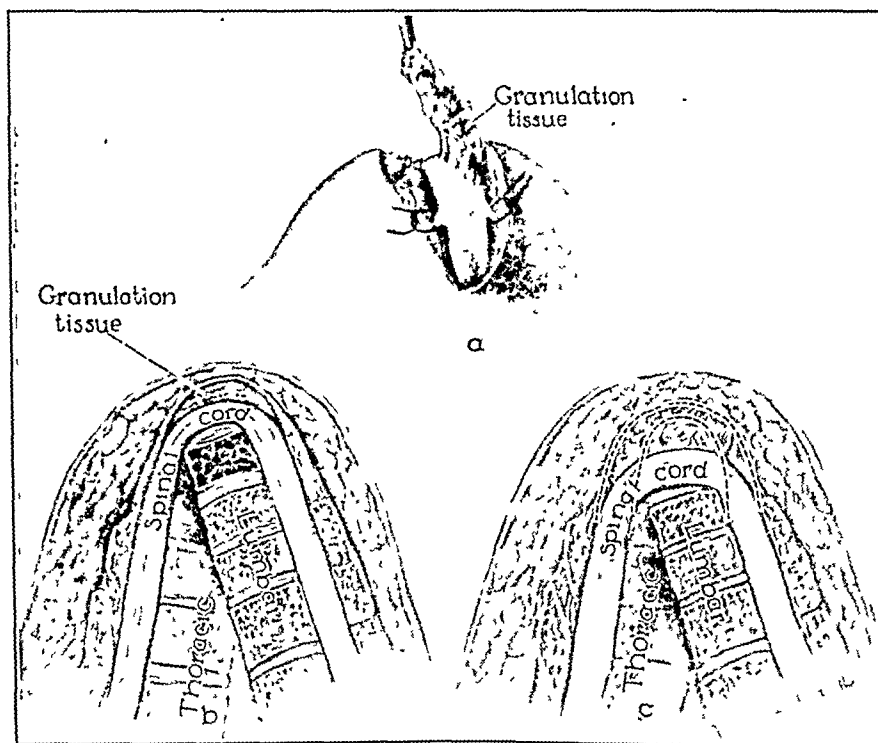


Fig. 3 (case 1).—The condition present and the surgical procedure which was carried out to relieve the compression of the spinal cord. (a) Removal of the extradural granulation tissue and ligation and division of nerve roots. (b) Sagittal plane showing the marked kyphosis and angulation and compression of the spinal cord between the granulation tissue and the diseased bone. (c) The spinal cord transplanted to a new position and thus relieved of pressure.

ment in the motor power of the left leg. In general, the examiner was of the opinion that considerable improvement had taken place. The patient was dismissed from the hospital fifteen days after operation. A written report from his family physician six months following the transplantation of the spinal cord stated that "he has completely recovered, is working and driving a car—no sequelae."

CASE 2.—This patient, a housewife 50 years old, registered at the clinic on June 30, 1947, with a complaint of soreness in her back and inability to walk. She stated that she had been well until three and a half years before, when an aching pain developed in her back. Within three months she noticed weakness in

her legs. Rest in bed for nine months effected a cure for a year. Six months prior to registration she again noticed a gradual loss of sensation and strength in her legs. On admission she had spastic paralysis with absence of sensation below the tenth thoracic segment and increased reflexes (fig. 4). The Babinski sign was present bilaterally.

When a similar procedure was used as previously described, the granulation tissue was removed, an extradural abscess evacuated and a large bony ridge was removed in order to move the cord anteriorly. The tissue removed was considered by the pathologist to be tuberculous granulation tissue. The following day the patient noticed some improvement in her ability to move her legs, and for one week she continued to improve. At the time of her discharge, twenty-five days

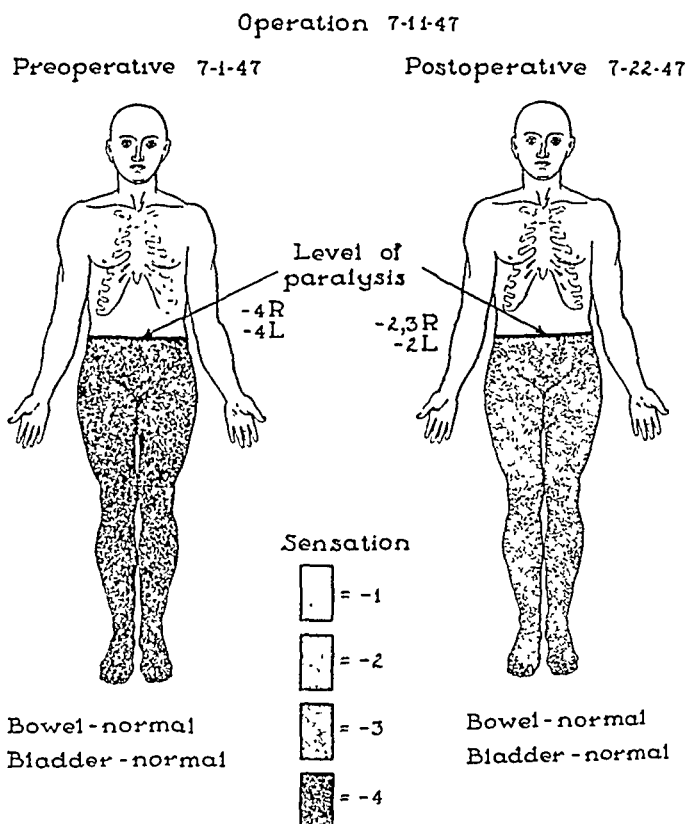


Fig. 4 (case 2).—The principal neurologic signs before operation and immediately after operation. A later follow-up revealed considerable improvement.

after operation, in spite of the use of streptomycin and rest in bed she had regressed to her former state of complete paraplegia. Because it seemed likely that her tuberculous lesion had flared up, she was advised to remain in bed for conservative treatment of the tuberculosis. Eleven months following the transplantation of her cord she wrote that strength, sensation and action were good in her legs, that she had no pain and that her general condition had improved greatly. Seventeen months after her operation roentgenologic examination of the thoracic vertebrae revealed recalcification and healing. She was then allowed to be up and was fitted with a Taylor brace.

CASE 3.—A boy, 11 years old, first registered at the clinic on Feb. 6, 1945. According to the history obtained, he had poliomyelitis at the age of  $1\frac{1}{2}$  or 2 years, although this was not diagnosed during the acute stage. There was also some question whether a birth injury would account for his back deformity. At the age of 6 years he was operated on for relief of flexion contracture of the right knee and afterward was able to get around well. Physical examination at the clinic showed marked kyphoscoliosis (fig 5) with deformity of the ribs. A



Fig. 5 (case 3) —The spinal column showing marked kyphoscoliosis which had been fused with bone grafts previously (anteroposterior view).

neurologic examination showed some weakness of the right leg and a more pronounced weakness of the left leg. Sensory perception was decreased in all modalities from a level of the sixth thoracic segment. He had increased reflexes in both legs as well as bilateral Babinski signs. It was felt that he had some intrinsic disease of the cord, the nature of which was not clear. For the next two years he was seen at the clinic at various intervals, during which time orthopedic procedures, including bone graft fusion, were carried out in an effort to correct his scoliosis. His neurologic status was not changed during these

visits. He returned in June 1947, at which time he stated that he had been getting along well until April, when pain developed in both legs while he was riding a bicycle. In several days this progressed to a complete spastic paralysis of both legs. Neurologic examination (fig. 6) at this time showed marked weakness of the abdomen and both lower extremities, with increased reflexes, ankle clonus and bilateral Babinski signs. The sensory level was felt to be between the fifth and seventh thoracic segments. Since lumbar and thoracic spinal punctures were unsuccessful, radiopaque oil was injected into the cisterna magna by one of us (J. G. L.). Roentgenoscopy revealed a block (fig. 7) at the level of the fifth thoracic vertebra.

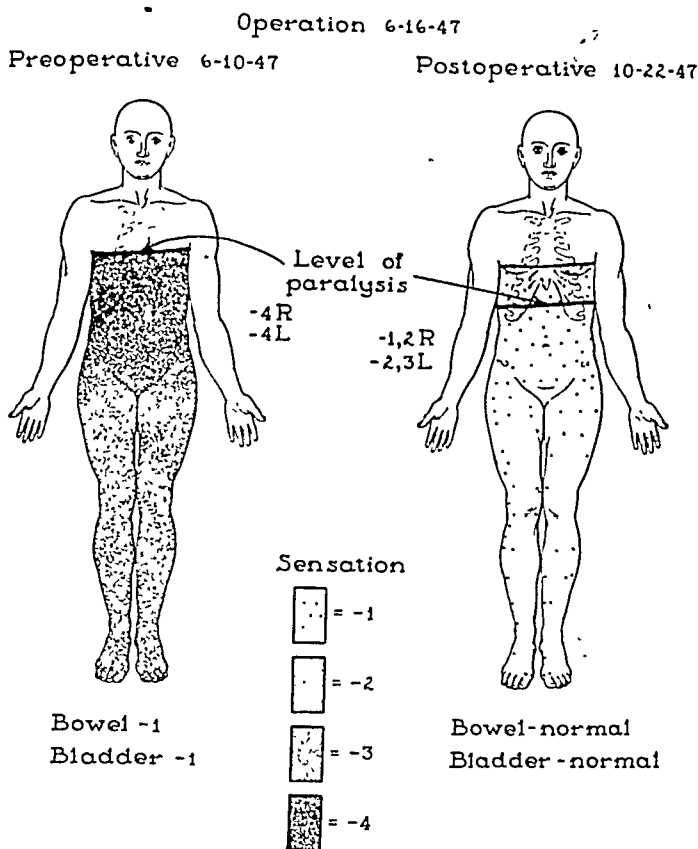


Fig. 6 (case 3).—The essential neurologic findings prior to operation and the marked improvement which was obvious four months later.

With the procedure previously described, it was found at operation that the cord was compressed at the level of the apex of the kyphos. When a portion of a bone graft previously placed along with the lamina was removed, normal pulsation of the spinal cord was resumed. A probe passed up and down the spinal canal revealed no further obstruction. There was no evidence of tuberculosis.

When the patient was reexamined two weeks later, no significant neurologic change could be detected, but on his return in October 1947, four months after operation, he could stand and his weakness was considerably less. There was no change in the sensory level, but there was some return of sensation in a patchy fashion in both lower extremities.

CASE 4.—The patient was a man, 22 years old, whose appearance and disease closely resembled that of the patient described in case 1. He registered at the clinic because of inability to walk, which had its onset about one year previously. According to the patient, he had sustained an injury at the age of 3 years which left his back and chest deformed. One year prior to registration he noticed pain in the right lower abdominal quadrant and right thigh. This lasted for about two weeks. Shortly thereafter he noticed some difficulty in ascending stairs due to weakness of his right leg, which progressed so that in three weeks he was unable to walk. This motor impairment remained stationary for the next nine months. He complained of no sensory disturbances, nor did he have any difficulty controlling his bowels or his bladder.



Fig. 7 (case 3).—Myelogram with the head up after injection of radiopaque oil showing complete block of the oil in the upper thoracic portion of the spinal canal.

Except for the injury mentioned, he had had no serious illnesses. At the age of 3 months he was closely associated with an aunt who had tuberculosis.

Examination revealed a small, thin man with marked kyphosis of the thoracic portion of the spinal column. Neurologic examination (fig. 8) showed moderate weakness of the left leg and marked weakness of the right leg. All deep reflexes were increased in the lower extremities; bilateral ankle clonus was present, and Babinski's signs were elicited bilaterally. Sensation was considered to be intact.

Except for mild anemia, laboratory studies showed nothing significant. Roentgenologic examination of the spinal column revealed pronounced thoracic kyphosis, which most probably was due to Pott's disease of the middle thoracic vertebrae.



It was felt the patient had marked compression of the cord in the thoracic region; hence exploration was advised.

One of us (J. G. L.), using the procedure previously described, transplanted the patient's spinal cord anteriorly after sufficient bone had been removed with a rongeur, chisel and cranial perforator from the posterior portion of the body of the vertebra which was displaced and was compressing the spinal cord. The abnormal tension of the spinal cord was thus relieved. A specimen of granulation tissue surrounding the spinal cord was submitted to the laboratory for smear, culture and guinea pig inoculations.

Immediately after the operation the patient's movements were extremely limited. He was capable of some slight motion in the right lower extremity and scarcely

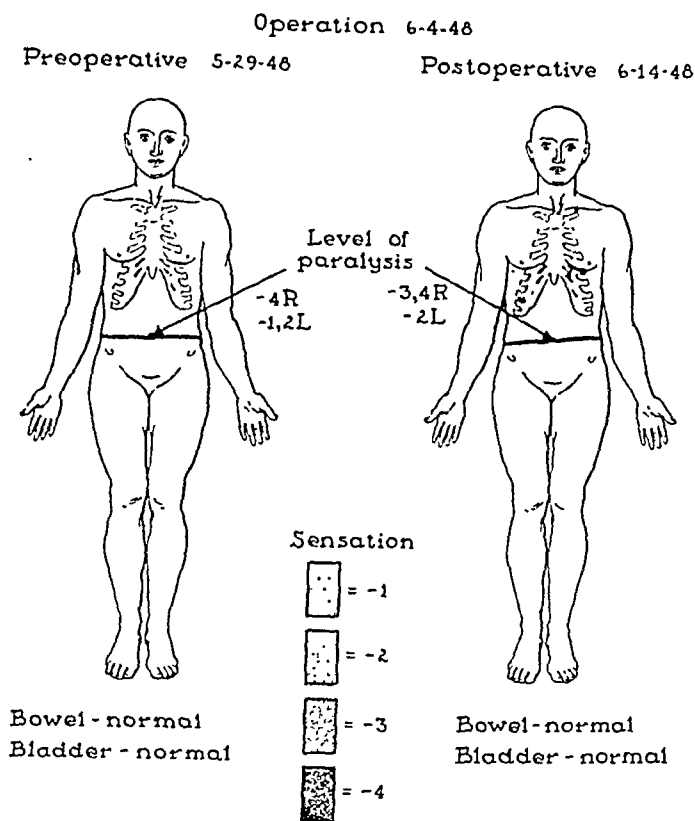


Fig. 8 (case 4).—The marked motor impairment without sensory loss before and after operation.

little more in the left. His temperature rose to 104 F., but nothing in his clinical condition seemed to indicate anything more serious than a febrile reaction to a blood transfusion. Several days later the patient was allowed out of bed, and after the lesion had been proved to be tuberculous he was treated with streptomycin. Neurologic examination ten days after operation showed almost complete paralysis of the right lower extremity and moderate weakness of the left. Signs indicative of a lesion in the pyramidal tract were present to about the same degree as before operation.

The wound was well healed in three weeks, at which time the patient was allowed to go home. Continuation of treatment with streptomycin for another three months was advised.

The next case is of interest in that no tuberculous process was present but a congenital anomaly of the thoracic portion of the spinal column was responsible for the paraplegia.

CASE 5.—This patient, a student 17 years old, registered at the clinic on Sept. 18, 1948, with the complaint of loss of function in both legs. He had apparently been well until the winter of 1947-1948, when he fell during a hockey game and shortly afterward noted that his left knee seemed to "give way" because of weakness. By June 1948, his legs were weaker, and in the next month the weakness progressed so that by August he was unable to walk without staggering. He was hospitalized elsewhere and found to have marked weakness and incoordination of both legs with increased reflexes and bilateral Babinski signs. The sensory level was at the third or fourth thoracic segment. Roentgenograms of the thoracic portion of the spinal column revealed the fifth thoracic vertebra to be a hemivertebra with the left side absent. Laminectomy was performed from the fourth to the sixth thoracic vertebra. Although the dura was seen to pulsate, the spinal cord was kinked. When the dura was opened, a catheter could readily be passed up and down the subarachnoid space. Because a tumor was not found, a bone graft was placed from the third to the sixth thoracic vertebra, inclusive. On examination after operation, complete paraplegia with the sensory level at the fifth thoracic segment was found. It was felt that postoperative edema had further damaged the already poorly functioning spinal cord. The paraplegia did not improve, but the patient did show a minimal amount of recovery of sensation within a week. (This information was furnished by the referring surgeon.)

The patient's family and past medical history were noncontributory to his present illness.

On examination at the clinic, the marked deformity of the thoracic portion of the spinal column with its convexity toward the right was obvious on inspection. No other abnormalities from a general standpoint were noted. Neurologically, the patient showed complete paraplegia and a sensory loss for all modalities below the nipple line (fig. 9). Reflexes were increased in the lower extremities; Babinski signs and ankle clonus were present bilaterally. The patient was incontinent of urine and feces. No evidence of tuberculosis or malignant disease could be found. Roentgenograms of the spinal column revealed a marked dorsal scoliosis with angulation at the level of the fifth thoracic vertebra. There were thirteen thoracic vertebrae and thirteen ribs on the right and only twelve on the left. The fifth vertebra was a hemivertebra with the left side absent. Evidence of the previous laminectomy and the bone graft were noted. Laboratory studies revealed the presence of albumin and pus in the urine but gave otherwise normal or negative results.

Inasmuch as the nature of the paralysis was felt to be indeterminate, all consultants who had seen the boy believed an exploration to be indicated.

Just prior to the exploration a lumbar puncture was performed, which revealed complete subarachnoid block. The total protein of the cerebrospinal fluid was 300 mg. per hundred cubic centimeters, and the cell count revealed 14 lymphocytes per cubic millimeter. With the patient in the face down position, one of us (J. G. L.) carried out costotransversectomy of the third, fourth and sixth ribs and corresponding vertebrae on the left side with lateral retraction of the left trapezius and rhomboid muscles and mesial retraction of the semispinalis muscles. The remaining portions of the third, fourth and sixth thoracic laminae on the left, along with the articular facets, pedicles and portions of the intervertebral disks, were removed in order to allow the angulated and compressed spinal cord to assume

a more nearly longitudinal course and also to move to the left. It thus obtained a shorter course than it could obtain in its old position, where it went over the apex of the scoliosis to the right. Likewise, it was considered that this procedure would allow the spinal cord to drop anteriorly and thus prevent its compression by the kyphotic vertebrae. The fourth and sixth thoracic nerve roots on the left were clipped with silver clips and divided because they were tense and tugged on the common dural sac. At the completion of these steps in the operation, the cord had straightened out satisfactorily, although pulsations did not go the entire extent of the operative site. The dura was thickened on the outside as though there had been some organization around it, but there was no evidence of tuberculosis. The dura was opened, and obliteration of the subarachnoid pathways due to adherence

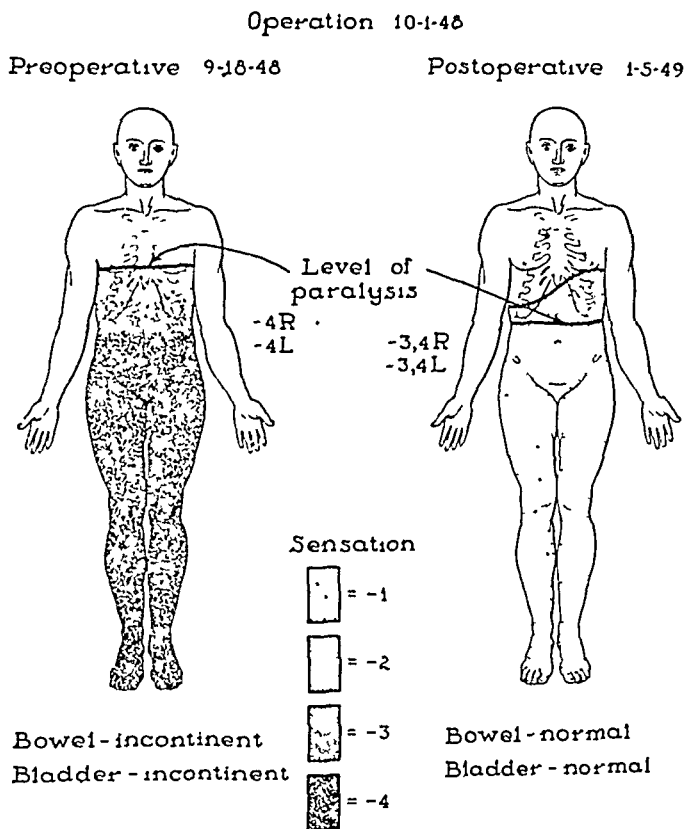


Fig. 9 (case 5).—The essential neurologic findings prior to operation and about four months after operation, at which time considerable improvement had occurred.

of the arachnoid and dura to the cord was noted. No cerebrospinal fluid was obtained on opening the dura and arachnoid; so it was left open for decompressive purposes. The previously placed bone graft was not disturbed.

The patient's postoperative course was rather uneventful. A minor infection of the urinary tract, which was easily controlled with chemotherapy, developed. The patient became afebrile by the fourth postoperative day, and the skin sutures were removed on the eleventh day. Physical therapy was given after the tenth postoperative day and in several weeks the patient's bowels and bladder were functioning properly. In six weeks he was allowed out of bed in a wheelchair with a Taylor spine brace for support. During this time repeated neurologic

examinations were made showing some slight improvement. The last examination, made approximately three months after operation, showed definite improvement in both motor strength and sensation. The patient was able to dorsiflex the toes of both feet, and, whereas previously sensation was diminished below the nipple line, he now was able readily to distinguish pain, touch and temperature in this region. His bowels and bladder were normally controlled.

#### COMMENT

In 3 of these cases acute paralysis developed some time prior to operation, while in 1 (case 1) surgical treatment was given soon after paraplegia developed. There is little comparison in the results.

Although it is only speculation to say that the 3 patients who had paraplegia for some time could have been relieved by prompter surgical treatment, it is significant that the patient who had paralysis of shortest duration recovered more promptly and completely after transplantation of the spinal cord. It can be pointed out also that with the advent of streptomycin one of the principal objections to exploration of a tuberculous process involving the spinal cord may be minimized.

#### SUMMARY

Five cases of anterior transplantation of the spinal cord are presented with the belief that this procedure has some value in the treatment of Pott's disease with associated paralysis. Likewise, it may prove useful in other conditions (cases 3 and 5) in which the pathologic process involves compression of the spinal cord by a bony ridge which interferes with normal conduction of nervous impulses.

ADDENDUM.—After this paper had been completed, our attention was called to that of Dott, N.: *Skeletal Traction and Anterior Decompression in the Management of Pott's Paraplegia*, *Edinburgh M. J.* 54:620, 1947.

# EPITHELIOMA OF THE LOWER LIP

## Evaluation of Dissection of Cervical Lymph Nodes

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THERE is considerable diversity of opinion regarding the treatment of the region of the cervical lymph nodes in the presence of labial and intraoral malignant lesions. As Wilson<sup>1</sup> pointed out, the lymphatic spread of cancer may vary according to the primary site and therefore the results should be studied in terms of the origin of the metastatic lesions. In this paper we shall present only the results of treatment of the neck in squamous cell epithelioma of the lower lip.

The trend in the treatment of cervical nodes, as Duffy<sup>2</sup> has pointed out, has progressed from radical surgical procedures, pioneered by Kocher, Cheattle, Bloodgood and Crile, through extensive use of radiation at some centers to a consideration of the two methods separately or in combination.

It is felt that metastatic lesions develop by lymphatic emboli rather than by direct extension.<sup>3</sup> Therefore, the treatment of the secondary lesion can be considered to be separate from that of the primary lesion and the intervening tissue does not have to be removed.

Kennedy<sup>4</sup> has pointed out that there has been no improvement in the death rate from carcinoma of the lip in the United States since the advent of radiation treatment of cervical nodes. There have been no reported five year cures in the literature in the past fifteen years

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Dr. Judd is from the division of surgery of the Mayo Clinic.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Wilson, H.: Results of the Treatment of Metastatic Carcinoma in the Cervical Lymph Nodes: A Collective Review of the Recent Literature, *Internat. Abstr. Surg.* **75**:403-413 (Nov.) 1942.

2. Duffy, J. J.: Cervical Lymph Nodes in Intraoral Carcinoma: Surgery or Irradiation? *Am. J. Roentgenol.* **39**:767-777 (May) 1938.

3. Quick, D.: Management of Cancer of the Mouth and the Cervical Lymphatics, *Am. J. Roentgenol.* **31**:366-377 (March) 1934.

4. Kennedy, R. H.: The Management of Lymph Nodes in the Neck—Metastatic from Carcinoma of the Mouth, *Ann. Surg.* **114**:813-819 (Nov.) 1941.

from the use of external radiation to the cervical nodes when metastasis has been established by biopsy.<sup>5</sup> Hayes' Martin<sup>6</sup> has reported a five year survival rate of 51.1 per cent when interstitial irradiation is used.

It is the consensus of most authors that when the cervical nodes are involved and considered operable surgical intervention is always indicated. Operability may be established by Duffy's<sup>2</sup> indication. In cases of inoperable cervical nodes the patient must be given whatever palliative treatment may give him symptomatic relief.

The controversial question remains then: "What treatment should be given the patient in whom the cervical nodes are not palpable or are palpable but are considered benign?" One school of thought is that of expectancy—to "wait and see." This attitude has been supported by Martin,<sup>6</sup> Duffy,<sup>2</sup> Quick,<sup>3</sup> Wile and Hand,<sup>7</sup> Howes and LaRosa,<sup>8</sup> Sugarbaker<sup>9</sup> and others; in accord with it, surgical treatment of the neck is not undertaken until cervical nodes are palpable and considered clinically positive for metastases. The other school of thought supports the so-called prophylactic neck dissection, in which surgical treatment of the neck of a limited degree is carried out in selected cases in which cervical nodes are or are not palpable and are considered clinically negative for metastasis. Blair, Brown and Byars,<sup>10</sup> Kennedy,<sup>4</sup> Figi,<sup>11</sup> Dixon,<sup>12</sup> Wangenstein and Randall,<sup>13</sup> Mayne,<sup>14</sup> and Brown and McDowell<sup>5</sup> have supported this view.

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5. Brown, J. B., and McDowell, F.: Treatment of Metastatic Carcinoma of the Neck, *Tr. South. S. A.* **55**:254-266, 1944.

6. Martin, H.: The Treatment of Cervical Metastatic Cancer, *Ann. Surg.* **114**:972-985 (Dec.) 1941.

7. Wile, U. J., and Hand, E. A.: Cancer of the Lip: Results of Therapy in Four Hundred and Twenty-Five Cases Followed from One to Ten Years, *J. A. M. A.* **108**:374-382 (Jan. 30) 1937.

8. Howes, W. E., and LaRosa, F. J.: Carcinoma of the Lower Lip: Interval Statistical Survey of the End-Results in All Cases Treated at the Brooklyn Cancer Institute, 1930 to 1939 Inclusive, *Am. J. Roentgenol.* **47**:39-49 (Jan.) 1942.

9. Sugarbaker, E. D.: The Surgical Problem of Cancer in Lymph Nodes, *Surgery* **18**:608-619 (Nov.) 1945.

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11. Figi, F. A.: Epithelioma of the Lower Lip, *Surg., Gynec. & Obst.* **59**:810-819 (Nov.) 1934.

12. Dixon, C. F.: Submental and Bilateral Submaxillary Dissection: Colostomy as First Stage in Operation for Carcinoma of Upper Part of Sigmoid; Exteriorization Operation for Sigmoidal Polyp, *S. Clin. North America* **15**:1303-1307 (Oct.) 1935.

13. Wangenstein, O. H., and Randall, O. S.: Treatment and Results in Carcinoma of Lip: Report of a Hundred and Thirty Cases, *Am. J. Roentgenol.* **30**:75-81 (July) 1933.

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Hayes Martin<sup>6</sup> pointed out that in only 4 (3 per cent) of 128 cases of cancer of the lip did cervical metastasis later develop and cited this low incidence of cervical metastasis as not outweighing the risk of prophylactic surgical treatment. Duffy<sup>2</sup> strongly supported this view. Others have reported a higher incidence of metastasis in patients in whom prophylactic neck dissections have been performed. Kennedy,<sup>4</sup> in a series of 64 cases of carcinoma of the lower lip, found metastasis in 9 instances (14 per cent). He stated that cervical metastases will occur in 20 to 25 per cent of such cases. Simmons and Daland<sup>15</sup> reported similar findings in 25 per cent.

Blair, Brown and Byars<sup>10</sup> expressed the belief that neither clinical examination nor the routine histologic examination of removed lymph nodes disproves the presence of carcinoma cells, and they added that "only the passage of time can disprove their presence." Kennedy emphasized that simply because the pathologist in a routine examination fails to find carcinoma in removed cervical nodes one may not always assume that no metastases are present.

Morrow<sup>16</sup> expressed the opinion that successful treatment depends on keeping ahead of the disease and that this best can be done by routine neck dissection, whether nodes are palpable or not. Taylor and Nathanson<sup>17</sup> emphasized that an adequate follow-up course is the determining factor in the decision for or against prophylactic neck dissection in many cases. There is no experimental evidence to support Quick's view that the normal nodes tend to act as a barrier to carcinoma cells and in some instances actually destroy a number of small metastases. In the opinion of Wile and Hand,<sup>7</sup> Moreland<sup>18</sup> and Martin,<sup>19</sup> prophylactic irradiation of the neck is unnecessary, since there is no real proof that small doses will destroy cancer. Slaughter<sup>20</sup> added that the light doses used accomplish nothing except to confuse the situation. Wile and Hand,<sup>7</sup> in a study of 425 cases of carcinoma of

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15. Simmons, C. C., and Daland, E. M.: The Results of Operations for Cancer of the Lip at the Massachusetts General Hospital from 1909 to 1919, *Surg., Gynec. & Obst.* **35**:766-771 (Dec.) 1922.

16. Morrow, A. S.: Cancer of the Tongue: A Report of One Hundred and Eighty-Seven Cases, With an Analysis of Ninety-Eight Treated Principally by Surgery at the New York Skin and Cancer Hospital Between 1917 and 1935, *Ann. Surg.* **105**:418-441 (March) 1937.

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18. Moreland, R. B.: The Treatment of Metastatic Carcinoma of the Neck, Secondary to Carcinoma of the Lip, *J. A. M. A.* **110**:1084-1087 (April 2) 1938.

19. Martin, H. E.: Treatment of Cancer of the Lip, *Am. J. Surg.* **30**:215-226 (Nov.) 1935.

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the lip, reported 40 per cent five year cures from suprahyoid dissections in cases in which there was evidence of carcinoma in the cervical nodes.

Newell<sup>21</sup> reported 390 cases of carcinoma of the lip and reported 80.9 per cent five year cures by excision of the primary lesion only in cases with no metastases clinically, 85.3 per cent by excision of the tumor and neck dissection in cases without metastases and 22.5 per cent five year cures in cases in which radical neck dissection was done because of metastases. Kennedy<sup>4</sup> reported a 26 per cent five year cure rate following neck dissection for proved cervical metastases. Wile and Hand<sup>7</sup> reported a 40 per cent five year survival rate in patients with clinical metastases after neck dissection. Figi<sup>11</sup> reported a 39 per cent five year survival rate. Hayes Martin<sup>6</sup> reported 5 cases of five year survival in 21 cases of cervical metastases from lesions of the lower lip treated by neck dissection. Slaughter's recent figure for carcinoma of the lip after neck dissection is 33 per cent five year cures.<sup>20</sup> His over-all figure is 70 per cent five year survival rate. Taylor<sup>22</sup> reported 58 per cent cures after neck dissection in patients with involved nodes secondary to carcinoma of the lip. The interval was not stated.

#### PRESENT STUDY

From Jan. 1, 1930 through Dec. 31, 1939 802 patients with squamous cell epithelioma of the lower lip were seen at the Mayo Clinic. A review of the cases was undertaken primarily to determine survival rates according to grade of malignancy and type of treatment to the neck. In 28 of the cases, when the patients were first seen at the clinic the lesions were considered inoperable and hopeless as to cure from any form of treatment. Treatment in these cases was palliative. The series which is evaluated in this paper is composed of the 774 nonpalliative cases, which represent 96.5 per cent of the total number of cases.

#### THE LESION OF THE LIP

Because Figi<sup>11</sup> earlier had noted a difference in behavior between the epitheliomas of the lip which had previously been treated and those which had not received treatment, this series was divided into a primary group—those that had not received previous treatment to the lip—and a secondary group—those that had received previous treatment to the lip. Four hundred and fifty cases (58.1 per cent) were in the primary group and 324 (41.9 per cent) in the secondary group. Of the latter group, in about a third previous surgical treatment (including cautery) had been given, in a third caustics and escharotics had been used and in a third radiation therapy had been given.

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21. Newell, E. T., Jr.: Carcinoma of the Lip: Clinical and Pathologic Study of Three Hundred and Ninety Cases, With Report of Five Year Cures, *Arch. Surg.* **38**:1014-1029 (June) 1939.

22. Taylor, G. W.: Evaluation of Regional Lymph-Node Dissection in the Treatment of Carcinoma, *New England J. Med.* **226**:367-371 (March 5) 1942.



Lesions of the lower lip were all graded according to the Broders method (grade 1 being the least and grade 4 the most malignant). The growths varied as to their activity, but most of them were of low or moderate activity. Forty-two and four-tenths per cent were grade 1; 39.4 per cent were grade 2; 12.1 per cent were grade 3, and 1.8 per cent were grade 4; in 4.3 per cent the grade was not stated.

Epithelioma of the lower lip is still predominantly a disease of males. Of the 774 patients, 763 (98.6 per cent) were males and 11 (1.4 per cent) were females. This corresponds closely to the sex incidence as previously reported in the literature. The ages of the patients varied from 13 to 87 years, with an average age of 56.7 years. Eleven per cent of the patients were less than 40 years of age, and 30.5 per cent were less than 50 years of age. The age incidence is shown in table 1.

TABLE 1.—*Age Incidence of Epithelioma of the Lower Lip*

Age, Years	Patients	
	Number	Percentage
13-19.....	1	0.1
20-29.....	12	1.6
30-39.....	73	9.4
40-49.....	150	19.4
50-59.....	235	30.4
60-69.....	179	23.1
70-79.....	101	13.0
80-87.....	23	3.0

The average duration of symptoms for the primary group was 18.9 months, for the secondary group 30.0 months and for the total series 23.7 months. The size of the lesion in the primary group was somewhat smaller than in the secondary group. The average size in the former was 1.5 cm. in diameter, whereas in the latter it was more than 2 cm. in diameter. Approximately 40 per cent of the lesions were on the right side of the lower lip, 40 per cent on the left and 20 per cent in the midportion. In 18 (2.3 per cent) of the cases a new lesion of the lower lip developed after the first epithelioma had been controlled. Forty-two patients (5.4 per cent) had multiple lesions on the lower lip when first treated. In 33 cases (4.3 per cent) recurrent lesions developed during the follow-up period, 24 (72.7 per cent) of these cases being in the secondary group. Incidentally, in 65 cases (8.4 per cent) malignant lesions other than of the lower lip are known to have developed during the follow-up period.

Treatment of the primary lesion of the lower lip at the Mayo Clinic is chiefly by excision with a scalpel, using either the V excision or the lip shave technic or a combination of the two with immediate or delayed plastic reconstruction of the lower lip, when this is indicated. Accord-

ingly, 738 (95.3 per cent) received surgical treatment for the primary lesion of the lip. Fourteen patients (1.8 per cent) received radiation therapy, and in 22 cases (2.9 per cent) no treatment was indicated because previous treatment of the lip had been satisfactory.

The risk of surgical treatment of the primary lesion of the lip is very slight. In the 738 cases there were 2 deaths, representing a hospital mortality rate of 0.27 per cent. One patient died on the sixth post-operative day of pulmonary embolism, while the other, a patient 77 years of age with old pulmonary tuberculosis, died on the nineteenth day after radon seeds had been implanted in the lesion of the lip.

#### CERVICAL DISSECTION

The hospital mortality rate for those patients receiving surgical treatment to the cervical nodes is correspondingly low. In the 357 cases in which bilateral suprahyoid neck dissection or bilateral suprahyoid

TABLE 2.—*Accuracy of Diagnosing Palpable Cervical Nodes in Epithelioma of the Lower Lip*

Group	Clinically Negative				Clinically Positive				Total			
	Total	Proved	Per Cent Correct	Per Cent Erroneous	Total	Proved	Per Cent Correct	Per Cent Erroneous	Clinically Diagnosed	Proved	Per Cent Correct	Per Cent Erroneous
Primary.....	25	23	92.0	8.0	12	7	58.3	41.7	37	30	81.1	18.9
Secondary.....	18	18	100.0	0	63	41	65.1	34.9	81	59	72.8	27.2
Both.....	43	41	95.3	4.7	75	48	64.0	36.0	118	89	75.4	24.6

neck dissection with a unilateral block dissection was performed there was 1 death, a mortality rate of only 0.28 per cent. This patient had clinically involved cervical nodes which made surgical treatment imperative. He was a poor surgical risk because of questioned pulmonary tuberculosis. He died on the fourteenth postoperative day of bronchopneumonia. There were no deaths in cases in which operations were done as prophylactic neck dissections. Hayes Martin<sup>6</sup> reported a neck dissection mortality rate of 2.4 per cent. Figi<sup>11</sup> has previously reported a mortality rate of 0.18 per cent from the Mayo Clinic.

Thirty-one per cent of the patients had palpable cervical nodes, half of which were said to be small. In the primary group 20.7 per cent had nodes which were palpable, whereas in the secondary group, the nodes of 45 per cent were palpable.

#### ERROR IN DIAGNOSIS

The clinical diagnosis of metastatic involvement of cervical lymph nodes is not infallible. In the 118 cases in which the cervical nodes were definitely stated to be clinically negative or clinically positive, an

error of 24.6 per cent was proved after the tissue was removed and examined in the pathologic laboratory. This figure is broken down in table 2. Fortunately, the greatest error was in calling negative nodes positive for metastases. Duffy<sup>23</sup> stated that this error is between 15 and 35 per cent. When palpable nodes not stated to be either negative or positive are assumed to be negative, the clinical error in diagnosis is 20.1 per cent. As noted in table 3, of the total group 299 patients were stated to have clinically negative cervical nodes, palpable nodes considered negative or nonpalpable nodes. Of this number, 21 patients (7.0 per cent) proved to have metastases. In other words, 7 of 100 patients had metastases to the cervical nodes which were not diagnosed clinically. Jorstad,<sup>24</sup> who has stated that he prefers not to do a routine neck dissection but to wait for palpable nodes, found 66 per cent positive for metastases when neck dissection was done.

TABLE 3.—*Over-All Error in Clinical Diagnosis of Cervical Metastases in Epithelioma of the Lower Lip*

Nodes	Number	Negative	Positive	Percentage Positive
Clinically negative.....	43	41	2	4.7
Palpable, considered negative.....	90	77	13	14.4
Nonpalpable .....	166	160	6	3.6
Total.....	299	278	21	7.0

#### SURVIVAL RATES

Table 4 shows the survival rates according to grade of malignancy for traced patients for the five year and ten year intervals. It is interesting to note, as expected, that the survival rates are directly related to the activity of the lesion as expressed in grade; for example, the lower the grade of the lesion the better the survival rate. There is also a definite variation between the primary and the secondary groups. Those patients who had not received previous treatment to the lesion of the lip have a 9 per cent better survival rate in the five year period than the group that had received some previous treatment. In the ten year period the rate for the primary group is 10.2 per cent better than that for the secondary group. The five year survival rate for the total series is 79.3 per cent and the ten year rate is 61.8 per cent.

The five year and ten year survival rates according to type of treatment to the neck are shown in tables 5 and 6. The patients not receiving

23. Duffy, J. J.: Treatment of Cervical Nodes in Intra-Oral Cancer, Surg., Gynec. & Obst. **71**:664-671 (Nov.) 1940.

24. Jorstad, L. H.: Diagnosis, Treatment and Prognosis of Carcinoma of Buccal Mucosa, South. M. J. **35**:970-973 (Nov.) 1942.

TABLE 4.—*Survival Rate of Epithelioma of the Lower Lip According to Grade of Malignancy*

Grade of Malignancy of Labial Lesion	Patients *		Lived Five Years or More After Treatment		Patients *		Lived Ten Years or More After Treatment	
			Percentage of Traced				Percentage of Traced	
	Total	Traced	Number	Patients	Total	Traced	Number	Patients
<b>Primary group</b>								
Grade 1.....	234	197	170	86.3	194	132	93	70.5
Grade 2.....	169	150	125	83.3	151	123	82	66.7
Grade 3.....	39	34	24	70.6	37	27	16	59.3
Grade 4.....	5	5	3	60.0	5	5	1	20.0
Grade unstated	3	3	1	33.3	3	3	0	0
Total.....	450	389	323	83.0	390	290	192	66.2
<b>Secondary group</b>								
Grade 1.....	94	80	67	83.7	85	62	42	67.7
Grade 2.....	136	115	90	78.3	120	95	57	60.0
Grade 3.....	55	46	30	65.2	49	34	15	44.1
Grade 4.....	9	9	5	55.6	9	8	4	50.0
Grade unstated	30	27	13	48.1	24	19	4	21.1
Total.....	324	277	205	74.0	287	218	122	56.0
Total series.....	774	666	528	79.3	677	508	314	61.8

\* Inquiry as of Jan. 1, 1949. All patients are included in the five year group; the ten year group includes those patients treated in 1938 or earlier.

TABLE 5.—*Five Year Survival Rates of Epithelioma of the Lower Lip According to Type of Treatment to the Neck*

Type of Treatment	Patients Traced *	Lived Five Years or More After Treatment		Grades 1 and 2			Grades 3 and 4		
		Number	Percentage	Patients Traced *	Lived Five Years or More After Treatment		Patients Traced *	Lived Five Years or More After Treatment	
					Number	Percentage		Number	Percentage
Primary group									
No treatment.....	188	157	83.5	182	154	84.6	5	2	40.0
Prophylactic suprahyoid dissec- tion .....	131	112	85.5	105	93	88.5	26	19	73.1
Prophylactic irradiation.....	62	51	82.3	55	46	83.6	6	5	83.3
Suprahyoid + block dissection	7	3	42.9	5	2	40.0	2	1	50.0
Irradiation .....	1	0	0	0	0	0	0	0	0
Total .....	389	323	83.0	347	295	85.0	39	27	69.2
Secondary group									
No treatment.....	68	56	82.4	60	51	85.0	4	3	75.0
Prophylactic suprahyoid dissec- tion .....	147	120	81.6	106	91	85.8	31	24	77.4
Prophylactic irradiation.....	20	11	55.0	15	9	60.0	4	2	50.0
Suprahyoid + block dissection	37	17	45.9	13	6	46.1	13	6	46.2
Irradiation .....	5	1	20.0	1	0	0	3	0	0
Total .....	277	205	74.0	195	157	80.5	55	35	63.6
Total series.....	666	528	79.3	542	452	82.8	94	62	66.0

\* Inquiry as of Jan. 1, 1949. There were 30 cases in which the grade of malignancy was not stated.

treatment to the neck had small lesions of short duration, low cellular activity as a rule and little or no inflammation of the lip. In this group it is felt that the treatment to the primary lesion adequately controls the disease. Included in the group with a "prophylactic suprahyoid dissection" are those who received bilateral resection of submaxillary and submental nodes with or without the removal of the deep upper cervical nodes. In patients receiving prophylactic irradiation preoperatively or postoperatively to the labial lesion, prophylactic neck dissection was not felt to be indicated or the patients refused neck

TABLE 6.—Ten Year Survival Rates of Epithelioma of the Lower Lip According to Type of Treatment to the Neck

Type of Treatment	Lived Ten Years or More After Treatment			Grades 1 and 2			Grades 3 and 4		
				Lived Ten Years or More After Treatment			Lived Ten Years or More After Treatment		
	Patients Traced *	Number	Percentage	Patients Traced *	Number	Percentage	Patients Traced *	Number	Percentage
<b>Primary group</b>									
No treatment.....	133	88	66.2	120	88	68.2	3	0	0
Prophylactic suprahyoid dissection	108	78	72.2	85	64	75.3	23	14	60.9
Prophylactic irradiation.....	43	24	55.8	37	22	59.5	5	2	40.0
Suprahyoid and block dissection..	5	2	40.0	4	1	25.0	1	1	100.0
Irradiation .....	1	0	0	...	..	....	..	..	....
Total .....	290	192	66.2	255	175	68.6	32	17	53.1
<b>Secondary group</b>									
No treatment.....	48	28	58.3	44	27	61.4	2	1	50.0
Prophylactic suprahyoid dissection	121	80	66.1	89	64	71.9	22	12	54.5
Prophylactic irradiation.....	17	6	35.3	12	4	33.3	4	2	50.0
Suprahyoid and block dissection..	28	8	28.6	11	4	36.4	11	4	36.4
Irradiation .....	4	0	0	1	0	0	3	0	0
Total .....	218	122	56.0	157	99	63.1	42	19	45.2
Total series.....	508	314	61.8	412	274	66.5	74	36	48.6

\* Inquiry as of Jan. 1, 1949. Included here are only those patients treated in 1938 or earlier. There were 22 cases in which grade of malignancy was not stated.

dissection. This group also includes those patients requesting roentgen treatment. We do not feel that the amount of external radiation given in these cases is of any therapeutic value. The group having a suprahyoid plus a unilateral block dissection all had metastases. In these cases the sternocleidomastoid muscle and the internal jugular vein were sacrificed on one side. The number receiving radiation alone is negligible.

The patients who had a prophylactic suprahyoid dissection have a better survival rate in the five year period than the group not receiving that treatment. These survival rates are substantially better than the rates for those receiving prophylactic radiation. Thirty-four patients, mostly in this group, were advised to have a prophylactic suprahyoid dissection but refused. In the ten year period patients in the primary

group having a suprahyoid dissection had a 6.0 per cent better chance of living than those having no such treatment and 16.4 per cent better chance of living than those receiving prophylactic radiation. This held true for the secondary group also. It is interesting to note that the survival rates in the secondary group are lower than in the primary group when determined according to type of treatment to the neck, as they also were when classified by grade of malignancy.

In 74 cases nodal metastasis was established by microscopic examination. This represents 9.6 per cent of the total cases. Twenty-one and six-tenths per cent of these were in the primary group and 78.4 per cent were in the secondary group. In 4 cases the tumor was of grade 1, in 22 of grade 2, in 19 of grade 3, in 9 of grade 4; in 20 the grade was not stated.

TABLE 7.—*Survival Rates of Patients with Epithelioma of the Lower Lip and Cervical Metastases*

	Lived Five Years or More After Treatment				Lived Ten Years or More After Treatment			
	Patients *		Num- ber	Per- centage of Traced Patients	Patients *		Num- ber	Per- centage of Traced Patients
	Total	Traced			Total	Traced		
Primary.....	16	16	7	43.8	14	14	5	35.7
Secondary.....	53	55	26	47.3	50	49	15	30.6
Total.....	74	71	33	46.5	64	63	20	31.7

\* Inquiry as of Jan. 1, 1949. All patients are included in the five year group; the ten year group includes those patients treated in 1938 or earlier.

The survival rates of patients with proved metastatic cancer are found in table 7. The five year rate of survival is 46.5 per cent, and the ten year rate is 31.7 per cent for these cases.

#### SUMMARY

For patients who have an epithelioma of the lower lip with clinical evidence of metastasis to the cervical lymph nodes, surgical intervention by bilateral removal of the submaxillary salivary glands and lymph nodes and the submental nodes and unilateral dissection of the upper deep cervical nodes on the involved side is indicated. Block dissection of the anterior triangle of the neck with removal of the sternocleidomastoid muscle and the internal jugular vein is carried out when the upper deep jugular nodes are involved or the suprahyoid mass is large.

Interstitial radiation is recommended when the nodes are considered inoperable or the lesion is grade 4.

Prophylactic irradiation is considered a placebo.

For patients without clinical evidence of cervical metastatic lesions but with palpable nodes considered negative or without palpable nodes, a prophylactic suprahyoid node dissection is recommended under certain conditions.

If the labial lesion is grade 1, neck dissection is not advised unless the lesion is of long duration, large, infected, with considerable inflammatory reaction about it and probably of secondary character.

The majority of metastatic lesions are grades 2 and 3; therefore prophylactic dissection of nodes is recommended in all these cases, except for a few patients whose age or general condition does not permit major surgical intervention. In an occasional case in which the grade 2 primary lesion is treated early and the lesion is small, neck dissection might be omitted.

In early grade 4 lesions prophylactic neck dissection may be done, but usually there has already been metastasis and the lesions frequently are inoperable.

#### CONCLUSIONS

The following factors support prophylactic dissection of cervical nodes: the high clinical error in diagnosis of metastasis to the neck; the opportunity for removal of early metastatic lesions which develop in approximately 10 per cent of epitheliomas of the lower lip; the prevention of metastasis by blocking off the lymphatics by surgical removal; the low mortality rate of the suprahyoid dissection; a high survival rate of patients so treated, and the impossibility of adequate follow-up examination in nonresident patients.

# NONOBSTRUCTIVE LATERAL PORTAL VEIN-VENA CAVA ANASTOMOSIS

A Clinical Application of the Smith Freeman Clamp

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THE APPLICATION of advancing methods of venous anastomosis to the problem of portal hypertension has demonstrated the value of surgical treatment in diminishing the dangers of hemorrhage secondary to this condition. Blakemore,<sup>1</sup> Whipple<sup>2</sup> and Linton<sup>3</sup> have explored the feasibility and value of a variety of methods and sites of the production of venous shunts between the portal system and the vena cava. Although Linton has reported apparent success in 2 cases, utilizing anastomosis between the superior mesenteric vein and the vena cava in 1 and between the inferior mesenteric vein and the left ovarian vein in the other, the majority of anastomoses have been splenorenal or from the portal vein to the vena cava. The operation most frequently reported has been anastomosis of the splenic vein to the left renal vein, end to side, after splenectomy. Less often an end to side anastomosis between the portal vein and the inferior vena cava has been accomplished. In 1 case Blakemore<sup>1b</sup> has done a side to side portal vein-vena cava shunt.

It would seem that the direct shunt between the portal vein and the vena cava would be more effective in reducing portal pressures when its accomplishment is not prevented by changes within or about the portal vein. However, the disadvantages that the portal vein is completely obstructed during the anastomosis and that the liver is deprived of portal flow by the shunt are considerable.

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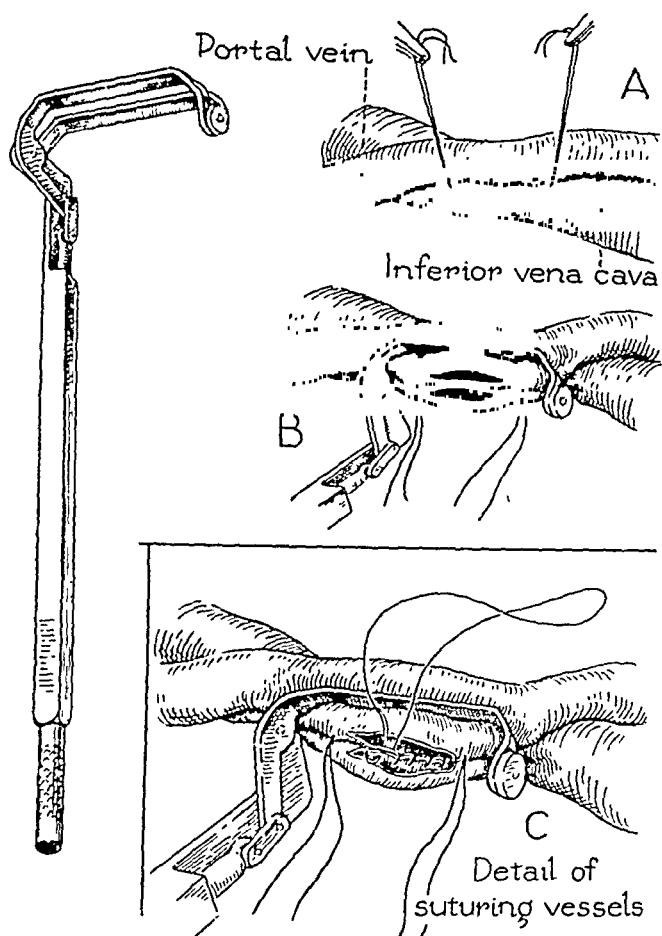
1. (a) Blakemore, A. H.: *Surg., Gynec. & Obst.* **85**:645, 1947; (b) *Ann. Surg.* **128**:825, 1948.

2. Whipple, A. O.: *Ann. Surg.* **122**:449, 1945.

3. Linton, R. R.; Hardy, I. B., Jr., and Volwiler, W.: *Surg., Gynec. & Obst.* **87**:129, 1948.



We have sought to overcome these disadvantages of direct anastomosis through the use of a new clamp devised by Smith Freeman.<sup>4</sup> This clamp, which was developed for Eck fistula studies in experimental animals, provides a means by which a side to side shunt between portal vein and vena cava may be made without obstructing either. Some of the difficulty encountered because of the plexus of veins in the hepatoduodenal ligament may be avoided because only



Construction of a side to side portal vein-vena cava anastomosis with use of the Freeman clamp (shown at the left). *A*, holding suture to mark the site of anastomosis; *B*, clamp in place and incisions made; *C*, placement of simple continuous suture.

the dorsal surface of the portal vein need be exposed. The line of anastomosis is selected where the two veins are in closest relationship and is demarcated by holding sutures at each end passed through all coats of both vessels and tied (figure, *A*). By careful traction on the stay sutures and compression of the vessels, the clamp is passed

4. Freeman, S.: Surg., Gynec. & Obst. 87:735, 1948.

down over the area of proposed anastomosis and tightly closed. The adjacent folds of vein are then opened longitudinally within the stay sutures and slightly medial to the apex of the fold (figure, *B*). The clamp, in its present form, does not provide room for an everting suture, and for this reason a simple continuous suture has been used (figure, *C*).

We have used this method clinically in the following case, with satisfactory results.

W. S., a 40 year old white male cab driver, was first admitted to the vascular surgical service of the Veterans Administration Hospital, Hines, Ill., in August 1948, because of gastrointestinal hemorrhage. Since 1940 attacks of weakness associated with tarry stools and hematemesis had occurred with increasing frequency and duration. In 1946 a splenectomy was done. The hemorrhages diminished in frequency for six months following splenectomy but returned to their preoperative severe degree. Laboratory examination on admission demonstrated a severe anemia, normal prothrombin time, normal excretion of sulfobromophthalein sodium, normal protein concentration and distribution and negative cephalin flocculation test. An attempt was made to sclerose the large esophageal varices which were seen at endoscopy, but this served only to increase the bleeding. After suitable preparation with blood transfusion, the patient was operated on on Sept. 16, 1948. Through a transverse subcostal incision, the duodenum was reflected medially, exposing the hepatoduodenal ligament and the vena cava. The portal vein was surrounded by a network of thin-walled veins which made its exposure difficult. The fact that only the dorsal surface needed to be exposed lightened the labor considerably. Tension in the portal vein was found to be 510 mm. of water. Anastomosis, 1 cm. in length, was accomplished with use of the Freeman clamp without event. The portal vein tension was then measured and found to be 400 mm. of water. There was no fluctuation of the arterial blood pressure in this interval. The patient recovered rapidly from his operation and was allowed early ambulation. The stools became negative for blood on the third postoperative day. The patient gained 20 pounds (9.1 Kg.) in weight in eight weeks following operation. During the ninth week he had a single tarry stool each day for three consecutive days but experienced no other symptoms. He did not report for examination at that time. Five months postoperatively his weight gain had continued, blood counts were normal and there had been no further evidence of bleeding. The biopsy specimen from the liver, taken at the time of the anastomosis, showed a marked increase in fibrous tissue with extensive areas of regeneration.

The production of an anastomosis between the portal vein and the vena cava, in those cases in which conditions do not prevent its use, has certain advantages over the less direct splenorenal anastomosis. A greater volume of blood flow can be obtained, depending only on the length of the anastomosis which is made. Avoidance of obstruction of the veins during the operation, particularly of the portal vein, is a theoretic advantage in that it may reduce the incidence of postoperative mesenteric thrombosis. The advantage that accrues from the use of a clamp of the design described is increased by the fact that the portal vein is only partially exposed.

The disadvantages of the method are that an everting mattress suture cannot be accomplished in the present clamp and that the surgeon is left without safety devices if mechanical failure should occur in the clamp. Slipping of the instrument has not been a factor, and the superior construction of the one now in use makes breakage or stripping of threads a most unlikely danger. The obvious changes which will permit the placing of a mattress suture have already been made, but the instrument of new design has not, at this time, been tested.

#### CONCLUSIONS

1. There are certain advantages inherent in a side to side portal vein-vena cava anastomosis.

2. A method for producing such an anastomosis without obstruction during the operation, previously described in animal experimentation by Freeman, has been used successfully in 1 clinical case.

## STERILITY AND ENDOMETRIOSIS

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**S**TERILITY is a common symptom of endometriosis. Various authors<sup>1</sup> have stated, as shown in table 1, that 20 to 66 per cent of the patients with endometriosis have a history of sterility. Pregnancy can occur in the presence of endometriosis, but the incidence is low.

Why are the majority of women who have endometriosis sterile? Witherspoon<sup>2</sup> stated that "the high frequency of sterility is due to the presence of the multiple follicular cysts of the ovaries in the absence of ovulation and subsequent formation of corpora lutea." This theory parallels that proposed as to the etiology of sterility in polycystic ovaries. This theory is not tenable for all cases, as the premenstrual phase changes characteristic of corpus luteum effect of endometrial transplants and corpora lutea have been demonstrated at operation, or in the removed ovaries. With or without the formation of a corpus luteum all cases of endometriosis of the ovaries have in common a disease process which develops in or on normal ovarian tissue. It must alter the normal blood flow and the normal intracapsular tension of the tissues of the ovary. With the recurring menstruation of the ectopic endometrium there would be produced and contained within the ovarian structures a normal or pseudonormal menstruum. There is a possibility that this menstruum or its subsequent degenerative products contain substances which might be reabsorbed by the tissues of the body and prevent the formation of an ovum, or of one incapable of being fertilized, or if fertilized, of being unable to implant itself on suitable endometrium.

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From the Department of Obstetrics and Gynecology, University of Nebraska College of Medicine.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. (a) Abell, I., Jr.: *Kentucky M. J.* **44**:339, 1936. (b) Counseller, V. S.: *Am. J. Obst. & Gynec.* **37**:788, 1939; *ibid.* **36**:877, 1938. (c) Fallon, J.; Brosman, J. T., and Moran, W. G.: *New England J. Med.* **235**:669, 1946. (d) Haydan, G. B.: *Am. J. Obst. & Gynec.* **43**:704, 1942. (e) Keene, F. E., and Kimbrough, R. A., Jr.: *Endometriosis: Review Based on Study of One Hundred and Eighteen Cases*, *J. A. M. A.* **95**:1164 (Oct. 18) 1930. (f) Smith, V. S.: *Am. J. Obst. & Gynec.* **17**:806, 1929. (g) Turunen, A.: *Acta obst. et gynec. Scandinav.* **19**:477, 1939.

2. Witherspoon, J. T.: *Clinical Pathological Gynecology*, Philadelphia, Lea & Febiger, 1939, p. 234.

Smith and Smith<sup>3</sup> have shown that the normal menstrual flow contains substances toxic to the experimental animal. Would it be too much to postulate that some substance produced by the ectopic endometrium could be toxic to the ovum?

Since endometriosis is a cause of sterility, it would reasonably follow that the removal of the ectopic endometrium and its by-products would cure the sterility.

Curtis<sup>4</sup> states that "few patients with extensive endometriomatous lesions become pregnant after conservative surgery, and even after satisfactory operation these patients tend to remain permanently sterile."

TABLE 1.—*Reported Incidence of Sterility Among Patients with Endometriosis*

Author	%
Abell <sup>1a</sup> .....	50
Counseller <sup>1b</sup> .....	32
Fallon <sup>1c</sup> .....	63
Haydan <sup>1d</sup> .....	53
Keene & Kimbrough <sup>1e</sup> .....	40.9
Smith <sup>1f</sup> .....	20.6
Turunen <sup>1g</sup> .....	45

TABLE 2.—*Reported Incidence of Pregnancy Following Conservative Operation*

Author	No. Cases	Pregnancy,	%
		No.	
Whorton <sup>5d</sup> .....	4	3	75
Counseller <sup>1b</sup> .....	55	7	12.7
Cattell <sup>5a</sup> .....	21	3	14.2
Payne <sup>5b</sup> .....	73	13	17.8
Keene & Kimbrough <sup>1e</sup> .....	14	4	28
Turunen <sup>1g</sup> .....	84	26	31.7
Schmitz & Towne <sup>5c</sup> .....	47	11	23.6
Total.....	298	67	22.4

Various authors<sup>5</sup> have stated, as is shown in table 2, that 13 to 75 per cent of the patients operated on become pregnant.

A careful analysis of these reports reveals that the following factors have not always been taken into consideration: (1) type of operation, (2) fertility of the husband, (3) desire for pregnancy, and (4) presence of other factors which of themselves might be factors in producing sterility.

3. Smith, O. W., and Smith, G. V.: *Proc. Soc. Exper. Biol. & Med.* **55**:285, 1944.

4. Curtis, A. H.: *Text Book of Gynecology*, ed. 5, Philadelphia, W. B. Saunders Company, 1946, p. 555 and p. 557.

5. (a) Cattell, R. B., and Swinton, N. W.: *New England J. Med.* **214**:341, 1936. (b) Payne, F. L.: *Am. J. Obst. & Gynec.* **39**:373, 1940. (c) Schmitz, H. E., and Towne, J. E.: *ibid.* **55**:583, 1948. (d) Whorton, L. R.: *South M. J.* **22**:267, 1929. (e) Counseller.<sup>1b</sup> (f) Keene and Kimbrough.<sup>1e</sup> (g) Turunen.<sup>1g</sup>

1. *Type of Operation.*—In some cases the disease process is so extensive that complete removal of both ovaries or all pelvic organs is necessary and pregnancy could not be expected to occur. In some instances associated pelvic lesions, such as leiomyoma of the uterus, necessitate additional surgical procedures to the extent that the reproductive ability of the patient is destroyed. Only those cases in which the uterus, tubes and enough ovarian tissue for ovulation can be conserved should be considered in the subsequent statistics on "pregnancy possible."

2. *Fertility of the Husband.*—In any survey of sterility the husband is found to be the causative factor in about 30 per cent of cases. In the 18 cases reviewed in this paper the semen of all the husbands was examined prior to the wife's operation. In 3 instances, or 16.6 per cent, the semen was aspermatic. In the existing circumstances pregnancy could not be expected in these 3 cases.

3. *Desire for Pregnancy.*—Three patients with pelvic endometriosis, not included in the present series of 18, were seen and operated on for acquired dysmenorrhea and the reproductive function conserved. When informed that there was a possibility of pregnancy after the operation, all three couples requested contraceptive advice. One of the patients in the present series practiced voluntary contraception for six years before attempting a pregnancy. The practice of voluntary birth control procedures should be taken into consideration in estimating percentages of pregnancy following surgical measures.

4. *Presence of Other Factors Which Might Produce Sterility.*—It has been frequently observed that in many instances of sterility several factors might be present, that each might be a cause of sterility and that the eradication of one factor might not necessarily result in a pregnancy. Cervical erosions, cervical stenosis and hypothyroidism might be, and have been, present in sterile women having endometriosis. Unless these additional factors are treated, an adequate operation for endometriosis may not bring about the hoped-for pregnancy.

Eighteen cases of pelvic endometriosis with a primary or chief complaint of sterility have been studied and are here presented. Dysmenorrhea was present in 3 cases but was not marked. In all 18 complete sterility studies were done on both the husband and the wife.

As mentioned previously, in 3 cases the husbands were found to be sterile. Enough abnormalities were found in the pelvis on pelvic examination in the 3 women to warrant operation, but no promise of subsequent pregnancy was offered.

In the remaining 15 cases operation was undertaken with the hope of a subsequent pregnancy. In addition, all the other possible sterility factors were treated. Eight, or 53.3 per cent, of the patients have become pregnant.

There have been to date 7 full term pregnancies and 1 abortion; 3 women are now pregnant, making a total of 11 pregnancies. One patient became pregnant three times, 1 two times and the other 6 once each.

One patient practiced voluntary contraceptive measures for six years and her husband was overseas in the Army for two and one half years; yet, after his return home she became pregnant in six months when all restrictions were removed. The interval otherwise between operation and the onset of a pregnancy varied from two to ten months, the average being seven months.

TABLE 3.—*Summary of Cases of Patients Becoming Pregnant*

Case No.	Age	Date	Treatment	Time for Pregnancy, Mo.	Outcome
1*	25	11/27/37	Right salpingo-oophorectomy	6	Boy 3/26/47
2	32	4/25/42	Right salpingo-oophorectomy; 75% resection of left ovary	6	Normal boy 10/8/43; normal boy 1/3/46; spontaneous abortion (2 mo.)
3	29	4/24/44	Resection of uterosacral ligaments; suspension of uterus	10	Normal girl 11/3/45
4	24	6/16/46	Resection of uterosacral ligaments; suspension of uterus	5	Boy 8/ ?/47
5	25	10/10/46	Left salpingo-oophorectomy; 50% resection of right ovary; suspension of uterus	5	Girl 12/3/47; pregnant; E.D.C.† 5/5/49
6	26	11/21/46	50% resection of left ovary; suspension of uterus	6	Boy 2/2/48
7	27	9/16/47	50% resection of both ovaries; phenol cauterization of vaginal cul-de-sac implants; suspension of uterus	10	Pregnant; E.D.C. 4/23/49
8	28	5/10/48	50% resection of left ovary; resection of uterosacral ligaments; suspension of uterus	2	Pregnant; E.D.C. 4/23/49

\* Practiced voluntary contraception for 6 years because of economic reverses; husband was then in the armed forces for 2½ years.

† Estimated date of confinement.

#### TREATMENT

The patient with a primary complaint of sterility and for whom a diagnosis of endometriosis is made deserves a very complete and careful sterility study. All factors which might play any part in the problem should be evaluated and corrected. The husband should be thoroughly checked before any surgical therapy is attempted for the patient.

At operation the surgeon will be presented with varied and perhaps difficult problems. He should be as radical as necessary but conservative enough to preserve the reproductive capacity of the patient. Partial resection of the ovary or ovaries should be done even if only a small portion of ovarian tissue remains. If one ovary is so badly involved that resection is impracticable and the other ovary is also involved, partial resection of that ovary is almost mandatory.

This is perhaps a controversial point. Payne <sup>5b</sup> has stated, "Conservation, particularly in young patients with preservation of ovarian and if possible menstrual and procreative functions is justified by the results." Curtis <sup>4</sup> condemns conservation on the basis that such "conservation may be followed by a secondary cystic swelling or inadequate estrogenic function from a fragment of ovary may eventuate in endlessly prolonged menopausal symptoms." When reproduction is the goal, the objections of Curtis can be overruled.

The cortex of the ovary should be preserved, and all sutures should be of very fine surgical gut. The uterosacral ligaments are frequently the seat of endometriosis. Resection of these ligaments is not too difficult and should be done.

TABLE 4.—*Summary of Cases of Patients Not Becoming Pregnant*

Case No.	Age	Date	Treatment	Comment
9	27	6/15/41	50% resection of both ovaries	Unable to find cause of continued sterility
10	29	6/ 7/46	Left salpingo-oophorectomy; 30% resection of right ovary	Hysterogram 3/29/47 showed nonpatent tube
11	31	5/15/47	Right salpingo-oophorectomy; suspension of uterus	Unable to find cause of continued sterility
12	27	3/ 3/48	Resection of both uterosacral ligaments	Basal metabolic rate —27%; taking thyroid, 0.13 Gm. daily
13	27	7/20/48	Resection of both uterosacral ligaments	Using contraceptives; husband has returned to school; patient has to work
14	37	7/24/48	Left salpingo-oophorectomy; 25% resection of right ovary	Uterus had several small fibroids; patient had mild depression after operation; no pregnancy yet attempted
15	30	9/25/48	Right salpingo-oophorectomy; 40% resection of left ovary; suspension of uterus	

Retroversion, frequently due to pelvic adhesions subsequent to endometriosis, is to be corrected by a method which will correct the condition and not interfere with a subsequent pregnancy and not permit recurrence of the retroversion following delivery. Suspension of the uterus should be a part of the operative procedure in those instances in which, in the opinion of the operator, postoperative adhesions might form and produce a retroversion.

No patients with endometriosis and a chief complaint of sterility have been treated by me with either high voltage roentgen therapy or testosterone. Payne <sup>5b</sup> reported that there were no pregnancies in his group of patients treated with high voltage roentgen rays. Schmitz and Towne <sup>5c</sup> reported 2 pregnancies in 12 patients treated with irradiation sufficient to produce temporary menolysis. Androgen therapy was also used by Schmitz and Towne <sup>5c</sup> in 15 cases with the idea of carrying



the patient as long as possible before instituting severe procedures. One patient became pregnant,

In my cases an interval of one month was placed on postoperative sexual abstinence. After this initial month, normal sexual relationship was resumed and a pregnancy attempted.

Experience with normal patients and with patients subjected to operation for cure of sterility due to pelvic abnormalities, such as polycystic ovaries or fibromyoma, reveals that the greatest number of pregnancies occur in the fourth to the seventh month after the initiation of coitus. In the present series, the onset of pregnancy occurred on the average at the sixth month after operation or the fifth month after the resumption of normal coitus. Patients should be warned of the time lag, and their mental outlook will be benefited if they realize that a pregnancy will probably not occur immediately. If it does occur earlier than the average, no harm will be done.

An analysis of the cases of the 7 patients that have not as yet become pregnant is presented in table 4; in cases 16, 17 and 18 the husbands were aspermatic.

#### SUMMARY

Eighteen cases of endometriosis with sterility as a chief complaint have been reviewed. Conservative operation with preservation of the menstrual and reproductive functions was possible in all cases.

When reproduction is the goal of the operation, resection of the ovaries, if they are involved, is justified, even if only a small portion of the ovary remains.

Additional resection of other areas of ectopic endometrium should be done and suspension of the uterus performed.

Further sterility studies revealed the husband to be the causative factor in 3, or 16.6 per cent, of the cases.

Of the remaining 15 cases, in 8, or 53.3 per cent, the patient has become pregnant; there has been a total of 11 pregnancies to date.

#### DISCUSSION ON PRECEDING PAPERS

DR. EGBERT H. FELL, Chicago: I wish to comment briefly regarding the very excellent presentation by Drs. Julian and Metcalf. In the past few months my colleagues and I have been using the same type of clamp in the experimental laboratories (on dogs) and in the necropsy laboratories and believe, as the authors do, that it is going to be a great help in the type of procedure that they have discussed. I am sure that it will cut down on the time interval which Dr. Blake-more and others have reported. I should like to ask that Dr. Julian state how long his procedure took. I believe, from our work in the laboratory, that the approach through the chest and abdomen would also be of help in this procedure. It, too, will give better access to the vessels, and with the aid of this new clamp the operation will be of shorter duration and much more easily accomplished.

DR. THOMAS C. DOUGLASS, Chicago: I agree entirely with what Dr. Julian and Dr. Fell said about the use of this clamp. My colleagues and I have been running an experiment recently on the cause of closure of these shunts in the laboratory, using the same clamp. It certainly is a very handy device and makes the operation very simple. I am not so sure that the disadvantage of the clamp mentioned by Dr. Julian—that is, the impossibility of using an everting type of suture in doing the anastomosis—is a disadvantage. Certainly, in the dogs we have had the healing of the shunt has been quite satisfactory. As a matter of fact, without obstructions of the portal vein proximal to the anastomosis, most of these shunts will close. If the portal vein is obstructed, however, they remain open for a prolonged period. I believe also that the approach through the abdomen, as Dr. Julian has shown, is quite a satisfactory approach, but we have not yet had the opportunity to do the operation on a human patient. I believe it can be done very simply and in much shorter time than has been reported by Blakemore and others.

DR. WALTER G. MADDOCK, Chicago: I should like to ask Dr. Ormond to say more about the treatment of the shock kidney. It is perfectly true that my experience in the past has been that in dealing with severe burns the administration of large amounts of fluid has often not resulted in a good urine output. On the other hand, it is a bit dangerous when considering any patient with oliguria or anuria not to consider a plentiful supply of water as the best diuretic. I am sure fluids are often pushed too far; hence I should like Dr. Ormond to tell just what measures should be taken to see that the patient has sufficient water and yet not too much.

DR. JOHN K. ORMOND, Detroit: First, I think it must be remembered that this concept of the lower nephron nephrosis is still not completely proved. It is still somewhat provisional, although we get more and more evidence in our pathologic studies and our autopsies that it is basically correct. If it is correct, the pouring in of fluids can do no good whatsoever. The necrosis of the cells of the ascending limb of the loop of Henle prevents the selective action of those tubes, and the fluid which is secreted or filtered by the glomeruli is passed down the tubes, just as it was before; but, since the power of selective resorption has been abolished, all that fluid is either poured back directly into the veins or resorbed into the veins, with the result that there is no possibility of the urine getting through. If that theory is correct—and it seems to have a great deal of backing—then in no circumstances in which this condition is present can the pouring in of the fluids do more than overload the circulation.

Another question was brought up, about burns. When I wrote my paper on this subject, I included thermal burns as one of the causes of this lower nephron nephrosis. Dr. Lam, who is a member of this organization at our hospital, said, "Burns do not cause this. What causes it is the tannic acid that has been used."

DR. WALTER G. MADDOCK, Chicago: Dr. Ormond, what are your indications for starting the use of the gastric lavage? When do you start it in the treatment, and just what methods do you use?

DR. JOHN K. ORMOND, Detroit: In a good many of our patients we have had to start gastric lavage on account of the presence of distention, etc., and the nasal tube is passed. We have taken advantage of that to use the gastric lavage. The chief indication, however, is the increasing toxemia. I do not believe that anybody knows when toxemia becomes dangerous. Nobody knows whether it is the nitrogen or the accompanying production of cellular metabolism that is poisonous. I only

know that the nitrogen acts as an indication, like the level of mercury in a thermometer. As I say, our experience is small. We pass the tube when the nonprotein nitrogen level is 100 mg. or a little higher. We do not pay much attention whether it gets down into the duodenum or whether it stays in the stomach. We inject fluids and then withdraw by suction, measuring the amount put in and the amount withdrawn, and then we subtract the amount withdrawn from the amount that was put in, and use that in our calculations of the amount of fluid that the patient is obtaining. In 1 patient we measured the nonprotein nitrogen content of the gastric lavage and found on one occasion that it was 66.5 mg. per hundred cubic centimeters. In another we found that it was 46.5 mg. These are the levels in the fluid extracted from the stomach by suction.

DR. O. C. JULIAN, Chicago: I want to thank Dr. Fell and Dr. Douglass for their comments. The approach through the abdomen is adequate in a thin person. Our patient was thin. If the patient is obese, and many of them are, I believe that the thoracoabdominal approach will be needed. The disadvantage of the thoracoabdominal approach in a patient with hepatic disease is that the liver will be enlarged occasionally, and there will be difficulty in displacing it up into the chest to expose its under surface. The time of operation was four and one-half hours in the case reported. I might say that we were misled in thinking that we had discovered a new syndrome. In palpating the liver and the tissues about the false ligament, a continuous bruit was palpated that was most striking, beyond any vascular bruit in a normal area that I had ever experienced, and much time was spent in trying to find an arteriovenous aneurysm.

I agree with Dr. Douglass that possibly the disadvantage of an over-and-over suture is overemphasized. However, one has only one opportunity in any patient to do this procedure, and I believe that the very best possible procedure would be to use an everting suture when it is made possible by a deeper clamp.

DR. J. GRAFTON LOVE, Rochester, Minn.: Patients such as Dr. Erb and I reported on are not encountered frequently and an operation will not be required very often, but when it is required it seems to me we have a procedure which will mean much to a few patients. I believe that it would be wise to administer streptomycin to these tuberculous patients before operation and to keep administering it to them for a long period afterward. How big a part streptomycin plays in the healing of the bone in these cases I do not know, but I think that we should give it credit for a good part of the successful outcome after the operation.

# SURGICAL TREATMENT OF TRICUSPID ATRESIA

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CARL B. DAVIS Jr., M.D.

AND

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CHICAGO

WILLIS POTTS and Sidney Smith<sup>1</sup> added an important chapter in the treatment of tetralogy of Fallot to that which Blalock and Taussig<sup>2</sup> so well began. The Potts-Smith operation, a lateral anastomosis of the pulmonary artery to the aorta, establishes an artificial ductus arteriosus, thus utilizing vessels that are accessible and large enough so that the infant under the age of 2 years who heretofore died of severe oxygen want now has a chance to live. It has been stated that there is a greater mortality in the group awaiting operation than in the operative and postoperative group.

The favorable results we have had with the Potts-Smith procedure in the age group from 4 to 12 months encouraged us to attempt this operation on 3 very small, cyanotic infants with diagnoses of congenital tricuspid atresia, or nonfunctioning right ventricle. There have been other cases of tricuspid atresia reported but we believe none in which operation was done at such an early age as in those to be reported here.

Congenital tricuspid atresia is rare.<sup>3</sup> There were 5 infants with this condition in the group of 135 with congenital cardiac anomalies studied in the children's cardiac service of the Cook County Hospital this past year. Thirty-three of the 135 anomalies were amenable to

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Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 18, 1949.

From the Cardio-Vascular Service of the Cook County Children's Hospital and the Laboratories of the Presbyterian Hospital.

1. Potts, W. J.; Smith, S., and Gibson, S.: Anastomosis of Aorta to Pulmonary Artery, *J. A. M. A.* **132**:627 (Nov. 16) 1946.

2. Blalock, A., and Taussig, H.: Surgical Treatment of Malformations of Heart in Which There Is Pulmonary Stenosis or Pulmonary Atresia, *J. A. M. A.* **128**:189 (May 19) 1945. Blalock, A.: Surgical Procedures Employed and Anatomical Variations Encountered in Treatment of Congenital Pulmonic Stenosis, *Surg., Gynec. & Obst.* **87**:385 (Oct.) 1948. Taussig, H. B.: Congenital Malformations of the Heart, New York, Commonwealth Fund, 1947.

3. Alexander, F., and White, P.: Four Important Congenital Cardiac Conditions Causing Cyanosis to be Differentiated from Tetralogy of Fallot; Tricuspid Atresia, Eisenmenger's Complex, Transposition of Great Vessels and Single Ventricle, *Ann. Int. Med.* **27**:64 (July) 1947. Abbott, M.: Atlas of Congenital Cardiac Disease, New York American Heart Association, 1936. Blackford, L. M.,

*(Footnote continued on next page)*

surgical correction; 3 of these were tricuspid atresia. The life expectancy is usually less than one year and depends on the patency of the ductus, anomalous arterial supply to the lungs and interauricular and interventricular septal defects. The success of the operation, likewise, depends on the continuance of the interauricular septal defect. An associated interventricular septal defect and patent pulmonary artery may also prolong life.

The blood flow in an infant with tricuspid atresia is from the right auricle through the interauricular septal defect to the left auricle, to the left ventricle and thence to the aorta (fig. 1). As long as the ductus arteriosus remains patent, blood will reach the lungs and the infant may appear normal, but as the ductus closes cyanosis increases in severity.

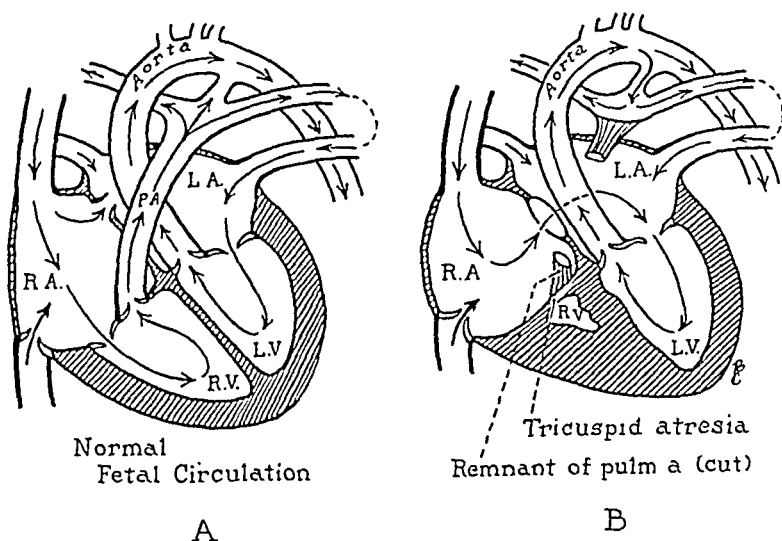


Fig. 1.—*A*, the normal fetal or newborn circulation; *B*, the circulation in the heart and great vessels in the presence of tricuspid atresia, interauricular septal defect and patent ductus arteriosus.

The diagnosis of nonfunctioning right ventricle is made by the appearance of cyanosis, which is usually seen earlier in infancy and is severer than that seen in an infant with the tetralogy of Fallot. Fluoroscopic examination reveals a boat-shaped heart of normal size with a small right ventricular shadow while the left ventricular shadow is increased; there is a pulmonary window and lack of pulmonary conus.

and Hoppe, L. D.: Functionally Two-Chambered Heart, *Am. J. Dis. Child.* **41**:1111 (May) 1931. Bellet, S., and Stewart, H. L.: Congenital Heart Disease: Atresia of Tricuspid Orifice, *ibid.* **45**:1247 (June) 1933. Gibson, S., and Clifton, W. M.: Congenital Heart Disease, *ibid.* **55**:761 (April) 1938. Taussig, H. B.: Analysis of Malformations of Heart Amenable to Blalock-Taussig Operation, *Am. Heart J.* **36**:321 (Sept.) 1948. Taussig, H. B.: Clinical and Pathological Findings in Congenital Malformations of Heart, *Bull. Johns Hopkins Hosp.* **59**:435 (Dec.) 1936.

The electrocardiogram shows a left axis deviation in contrast to the right axis deviation that is characteristic of the tetralogy of Fallot. The blood picture is similar to that in the tetralogy in that in both there is a marked increase in red blood cells and hemoglobin content and a low arterial oxygen content which is further diminished by the exercise test.

In the 3 cases to be reported there were all the diagnostic criteria (previously mentioned), and, in addition, the conditions were so severe that continuous administration of oxygen was essential for life from the time that the patient was first seen until operation was done. Parenteral



Fig. 2 (case 1) —Anterior-posterior view of the chest, showing clear pulmonary fields, boat-shaped heart, enlarged left ventricle and absence of the shadow normally caused by the pulmonary artery.

administration of food or fluids was necessary to overcome the frequent periods of unconsciousness that took place when food was given orally. All personnel who helped care for the infants believed that they would die at any moment.

We did not believe that operation would be possible; yet it held the only hope of providing the lungs with blood and affording an opportunity for life. The anesthesia was administered by Dr. F. M. Grem, chairman of the department of anesthesia of the Cook County Hospital, and the Potts-Smith procedure was completed without difficulty in each case. The anastomotic openings did not exceed 4 mm.

Postoperatively the patients were placed in oxygen tents for four or five days, and in due time were discharged to their homes with good color, gaining in weight and returning to normal activity for infants of their age.

#### REPORT OF CASES

CASE 1.—A 3 month old white boy was admitted to the cardiac service of the Cook County Children's Hospital on April 23, 1948, with the presenting complaint of cyanosis which was noted three days after a normal birth. His weight at birth was 5 pounds 3 ounces (2,355 Gm.). Seven and one-half weeks after birth, because of severe episodes of cyanosis, unconsciousness and marked dyspnea, he was hospitalized and oxygen was administered. He was transferred to the pediatric service of the University of Illinois on April 1, 1948.

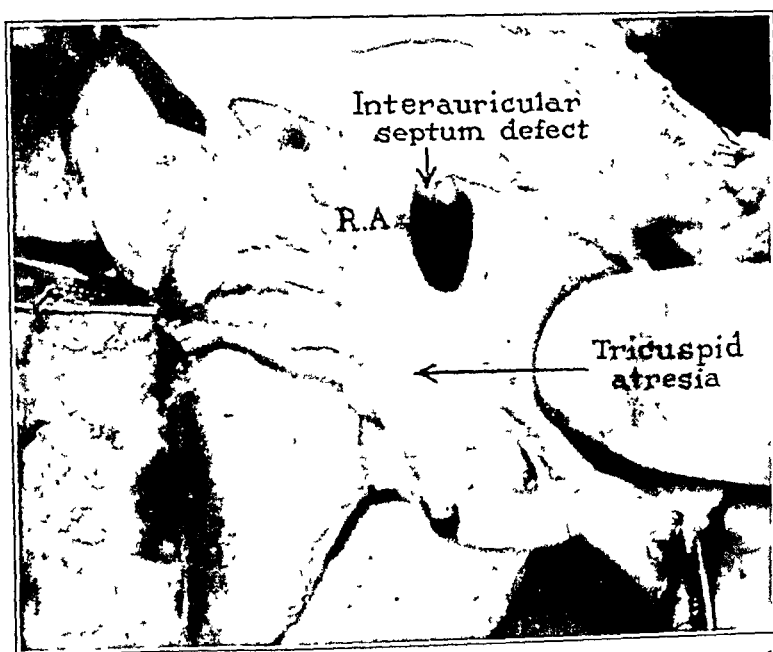


Fig. 3 (case 1).—A large interauricular septal defect leading from the right auricle is evident. There is no tricuspid valve or communication with the right ventricle. There was no evidence of failure of the right side of the heart.

Examination by one of us (B. M. G.) at this time revealed a 3 month old infant in distress, crying and gasping for air, with intense cyanosis of hands, feet, lips and mucous membranes. Respirations were 60 per minute with suprasternal retractions. The pulse rate was 160 and regular; the blood pressure was 76 systolic and 40 diastolic. The femoral pulse was present. Administration of oxygen did not completely relieve the cyanosis. The apex beat was in the fifth interspace, just outside the midclavicular line. There was a harsh systolic murmur, best heard in the second interspace on the left. There was no pulsation of the liver.

Fluoroscopic examination revealed the base of the heart to be markedly narrowed; there was a concavity in the region of the pulmonary conus with absence of pulmonary pulsations, and the pulmonary fields were clear. In the left oblique view, the left ventricle was definitely enlarged and the right ventricle

was small and was unusually distant from the anterior wall of the chest. The pulmonary window was wide and clear. There was a left aortic arch.

The electrocardiogram revealed a left axis deviation. Examination of the blood showed a hemoglobin content of 15 Gm., 7,970,000 erythrocytes and 10,650 leukocytes.

A diagnosis of tricuspid atresia was made, and the infant was transferred to the cardiac service of the Cook County Children's Hospital for further study and possible operation.

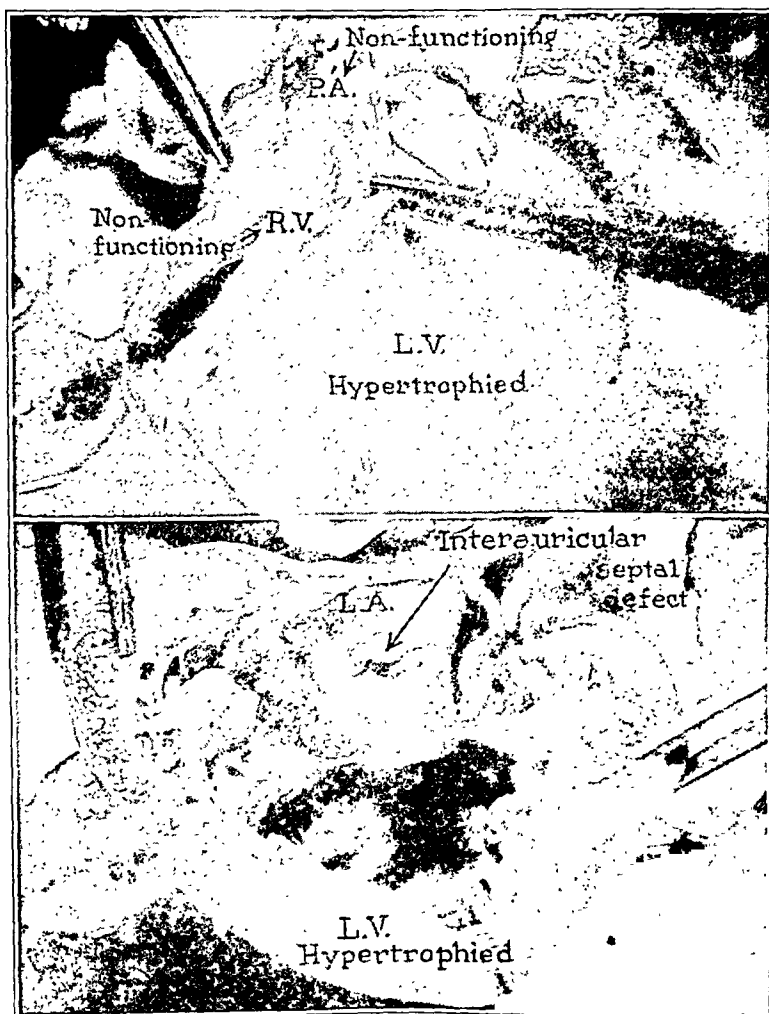


Fig. 4.—Upper illustration, a very small right ventricle is exposed, from which leads a small nonfunctioning pulmonary artery. There is no communication between the right ventricle and either the right auricle or the left ventricle. The left ventricle is noticeably hypertrophied. Lower illustration, the interior of the left side of the heart is shown. The interauricular septal defect is large and patent; the left ventricle is large and the wall hypertrophied.

Dextroangiocardigrams were interpreted as showing incomplete filling of the right ventricle, absence of a pulmonary artery and filling of the left auricle and of a large part of the left ventricle.

The diagnosis of tricuspid atresia with an interauricular septal defect, pulmonary stenosis and either a patent ductus or an interventricular septal defect was made.



From April 23 to July 2, the infant did very poorly, in spite of continuous administration of oxygen. Stimulants were used at times to aid in restoring consciousness.

Preoperatively, as in all cases of cyanosis, the patient was well hydrated. Atropine sulfate, 1/500 grain (0.4 mg.) preceded the cyclopropane-oxygen anesthesia. The chest was entered laterally through the fourth interspace. A quill-sized pulmonary artery was anastomosed to the aorta according to the method described by Potts and Smith. The anastomosis was 4 mm. in length. The



Fig. 5.—Upper illustration, the aortic arch has been opened, and a fine probe introduced into a small patent ductus arteriosus. Very little benefit was derived from this ductus. Lower illustration, the aorta distal to the left subclavian artery is opened and shows the artificial ductus between the aorta and pulmonary artery. The anastomosis was patent and appeared to have been functioning satisfactorily.

wound was closed in layers and the chest drained through a water seal for twenty-four hours.

The patient received 100 cc. of saline solution and 150 cc. of plasma during the operation; parenteral administration of food and fluids was continued for the first thirty hours, and thereafter he was fed by mouth. Oxygen was not

administered after the fifth postoperative day. On the sixteenth postoperative day he was found to have chickenpox and was transferred to the Contagious Division of the Cook County Hospital, where he made a successful recovery. He was discharged to his home on August 3, eating well, having good color and weighing 9 pounds 15 ounces (4,500 Gm.),  $1\frac{1}{4}$  pound (570 Gm.) more than he weighed when he was operated on. The stethogram showed the presence of a continuous murmur which could be easily heard, and the blood count was within normal limits.

The patient was seen at intervals in the outpatient clinic, and his color was noted to be normal and there was a satisfactory gain in weight and activity. On Jan. 15, 1949, a little over six months after operation, he was admitted to the Cook County Children's Hospital with severe bilateral bronchopneumonia and died within twelve hours of admission. Postmortem examination showed tricuspid atresia, a large interauricular septal defect, a ductus arteriosus with a very small lumen and a satisfactory-appearing artificial ductus between the aorta and the left pulmonary artery. There were pulmonary stenosis and hypertrophy of the left ventricle. There was no evidence of cardiac decompensation, endocarditis or aortitis, nor was there an interventricular septal defect.

From our postmortem studies, we believe that this patient with a completely nonfunctioning right ventricle and a large interauricular septal defect had an efficiently functioning heart and the cause of death was not related to the congenital cardiac condition or the surgical procedures associated with it.

CASE 2.—A  $5\frac{1}{2}$  week old white boy was admitted to the cardiac service of the Cook County Children's Hospital on July 21 1948, with the presenting complaints of dyspnea, rapid respirations of five weeks' duration and attacks of intermittent cyanosis of three weeks' duration.

His weight was 6 pounds  $7\frac{1}{2}$  ounces (2,900 Gm.) following a normal delivery. Labored rapid respiration was noted at this time. The physical examination revealed a  $5\frac{1}{2}$  week old cyanotic infant, weighing 6 pounds 11 ounces (3,034 Gm.), with severe dyspnea. Respirations were 70 per minute, pulse rate 160 and blood pressure 65 systolic and 25 diastolic. There was a marked cyanosis of all mucous membranes, fingers and toes and, to a slightly less degree, over the rest of the body. The femoral pulse was palpable.

The apex of the heart was in the fourth left interspace, just outside the mid-clavicular line. There was a harsh systolic murmur heard over the precordium. The liver was palpable, and at times a pulsation of its edge was questioned. The hemoglobin level was 18.5 Gm., the erythrocyte count was 6,500,000 and the leukocyte count was 12,000.

The fluoroscopic examination revealed in the posterior-anterior view a narrowing of the base of the heart. The pulmonary conus showed a straight, flat line. The pulmonary fields were unusually clear, with no pulsations of the pulmonary vessels. The left oblique view showed an enlarged left ventricular shadow and a diminished shadow in the right ventricular area. The pulmonary window was clear; the esophagram demonstrated a deviation associated with a normally placed aortic arch and descending aorta.

The electrocardiogram showed a sinus tachycardia and a left axis deviation.

A diagnosis of tricuspid atresia, or nonfunctioning right ventricle, with associated essentials—an interauricular septal defect and poorly functioning ductus arteriosus or an interventricular septal defect—was made.

In spite of continuous administration of oxygen, the infant had severe attacks of cyanosis and periods of unconsciousness. His cyanosis increased with age to a point that he could not take foods or fluids by mouth. With the use of blood and fluids intravenously, his weight was brought up to 7 pounds 1 ounce (3,200 Gm.) on August 6, the day of operation. Atropine sulfate  $1/480$  grain (1.2 mg.) was given preoperatively to aid in the administration of cyclopropane-oxygen intratracheal anesthesia. A Potts-Smith operation was completed through the fourth interspace of the left side of the chest; the anastomosis was 3 to 4 mm. in length. A good loud machine-like murmur was present directly

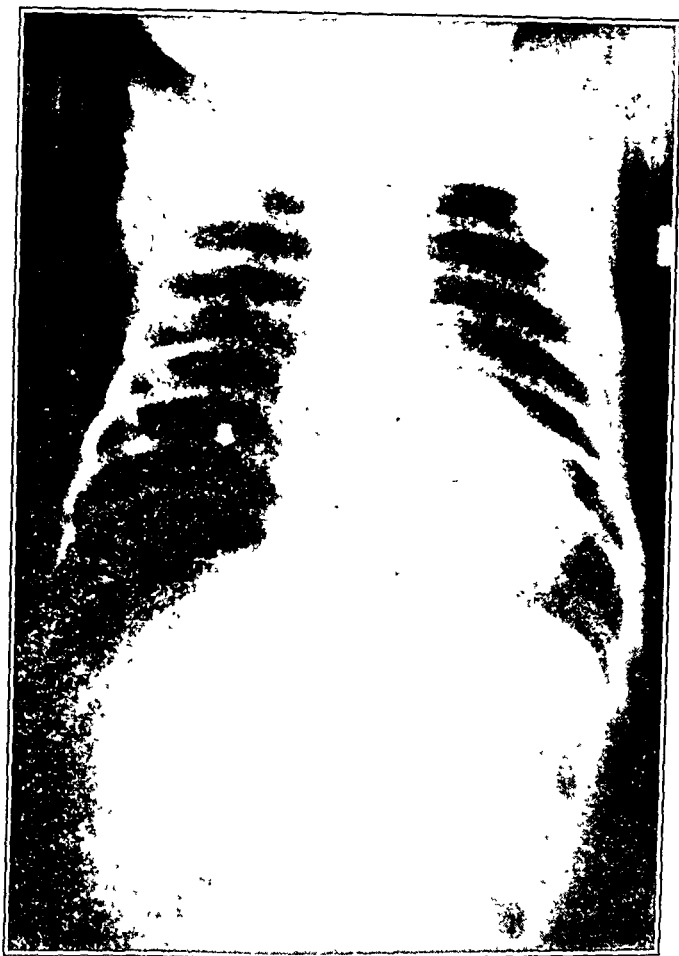


Fig. 6 (case 2).—Roentgenograms of the chest and esophagram of a  $7\frac{1}{2}$  week old infant. The esophagram gives evidence of a left aortic arch. The pulmonary fields are clear and free of pulmonary vessel markings. The heart is boatlike in shadow, and there is a lack of a pulmonary artery shadow.

after operation and the infant was put into an oxygen tent for four days; food was taken by mouth thirty-six hours postoperatively. He was discharged twenty-three days after operation, having gained in weight and with a normal blood picture. A continuous murmur was best heard to the left of the sternum in the fourth interspace.

CASE 3.—A 10 week old white boy was admitted to the cardiac service of the Cook County Children's Hospital on Feb. 13, 1949, very cyanotic. The child had been delivered by cesarean section and weighed 7 pounds  $6\frac{1}{2}$  ounces (3,360 Gm.).

Cyanosis was first noted at 3 weeks of age, at which time his physician stated that the infant had heart trouble. The cyanosis increased gradually, and on admission he had marked cyanosis associated with rapid respirations and cough, the last two complaints having been particularly noticeable in the past two weeks.

The physical examination showed a well developed baby weighing 9 pounds 8 ounces (4,310 Gm.). The marked cyanosis was increased in severity on crying or straining.

The lungs were clear. No cardiac murmurs were heard. The liver was not enlarged, nor was any pulsation of it noted. There was a good femoral pulse bilaterally. The respiration rate was 50 per minute, pulse rate 135 and temperature 98.3 F. The hemoglobin content was 16.5 Gm., erythrocytes 6,100,000, and leukocytes 12,250.

The roentgen and fluoroscopic examinations revealed a small right ventricle, a large left ventricle, a wide pulmonary window, decreased vascular markings and a concavity in the region of the pulmonary artery. The esophagram was compatible with a left aortic arch. The electrocardiogram revealed a left axis deviation and a sinus tachycardia.

The child was in a semicomatose state in spite of the fact that oxygen was continuously administered. Because of the favorable results in the 2 previous cases and the fatal termination if left alone, operation was advised. On Feb. 16, 1949, a 4 mm. anastomosis was made between the aorta and the left pulmonary artery. The infant made a spectacular recovery and was discharged thirteen days after the operation, weighing 1 pound (450 Gm.) more than at the time of operation and having a normal blood picture. The postoperative management and course were similar to those in the previous cases.

#### SUMMARY AND CONCLUSIONS

Three infants, aged 7½ weeks (weighing 7 pounds, 1 ounce), 5½ months (weighing 8 pounds) and 10 weeks (weighing 9 pounds, 1 ounce) with severe increasing cyanosis due to congenital tricuspid atresia were successfully operated on by the Potts-Smith procedure.

We do not advocate early operation for tetralogy of Fallot or tricuspid atresia unless it is evident that the patient will not survive conservative therapy. The 3 cases reported lead us to believe that we have waited too long and have been influenced too greatly by authors who have stated that operation should not be done before the age of 2 years. The Potts-Smith operation is a procedure that may be used on the very small infant. Time alone will tell whether this procedure will be of permanent benefit.

Severe cyanosis occurring in infancy associated with an enlargement of the left ventricle, diminution of the right ventricle and a left axis deviation as evidenced by the electrocardiogram are indicative of a tricuspid atresia. The life expectancy is less than one year. The group of patients with this defect is small but if the diagnostic criteria are kept in mind, relief is possible through surgical measures if there are no other congenital abnormalities to contraindicate an operative procedure.

## TRACHEOESOPHAGEAL FISTULA CAUSED BY BLUNT VIOLENCE

R. W. ALBI, M.D.

AND

R. K. GILCHRIST, M.D.

CHICAGO

THE PRESENT report deals with a case of tracheoesophageal fistula resulting from a severe blow over the sternum. This condition is extremely rare, and in a search of the literature only 2 similar cases with recovery were found. One of these, like the present case, presented no evidence of accompanying fracture of the ribs, cartilages or sternum. Both of the other cases were apparently reported twice.

The relative frequency of tracheoesophageal fistula based on etiology is furnished by Mangabeira-Albernaz,<sup>1</sup> who in 1933 studied 682 cases collected from the world literature. His classification of these fistulas is given in the table.

### REPORT OF A CASE

*History.*—On March 30, 1947, a 29 year old man was brought to the hospital by the police about fifteen minutes after injury. The patient stated that while driving home after having had some drinks he fell asleep at the wheel and his car struck the rear of a parked car. In the crash the steering wheel was broken by the impact of his chest. He had been in good health prior to his injury.

Physical examination revealed a well nourished white man of 29 years, alert, cooperative and not in shock. The blood pressure was 120 systolic and 80 diastolic. Temperature, pulse and respiration were normal. No significant abnormalities were noted except for pain on pressure over the left upper part of the thorax and persistent expectoration of bloody mucus. There was no bruise or abrasion anywhere on the thorax. Examination of the oral cavity and the nasopharynx did not reveal the source of bleeding.

*Diagnosis.*—It was thought at first that the patient had sustained fractured ribs and associated injury to the lung, and therefore treatment with penicillin, 20,000 units every three hours intramuscularly, was started. Roentgen examination of the chest revealed no abnormalities. It was later observed that whenever the patient attempted to take food or drink he was seized with paroxysms of coughing and vomiting. Roentgen examination of the chest during ingestion of iodized oil

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From the service of Dr. R. K. Gilchrist, Surgical Department, Cook County Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Mangabeira-Albernaz, P.: *Ann. d'oto-laryng.* 8:889 (Aug.) 1933.

U. S. P. (lipiodol®) demonstrated a communication between the esophagus and trachea in the region of the tracheal bifurcation.

*Management.*—It seemed that successful closure of the fistula in the present case depended, first, on control of infection at the site of injury and, second, on maintenance of nutrition and hydration. Use of penicillin was continued for three months. Fluid balance was maintained by parenteral administration of fluids at the beginning. Sodium sulfathiazole was given in the intravenous fluids intermittently. On the fifth day a Levin tube was passed into the stomach, and thereafter high protein, high vitamin feedings were given by tube.

*Progress.*—The patient did reasonably well on the management outlined, but some difficulties were encountered. On one occasion he vomited after a tube feeding, and shortly thereafter chill and fever (temperature up to 101 F.) developed. Fortunately, after removal of the Levin tube and treatment with intravenous injections of sodium sulfathiazole, the symptoms subsided. Also the

*Etilogic Classification of Tracheoesophageal Fistulas*  
(According to Mangabeira-Albernaz<sup>1</sup>)

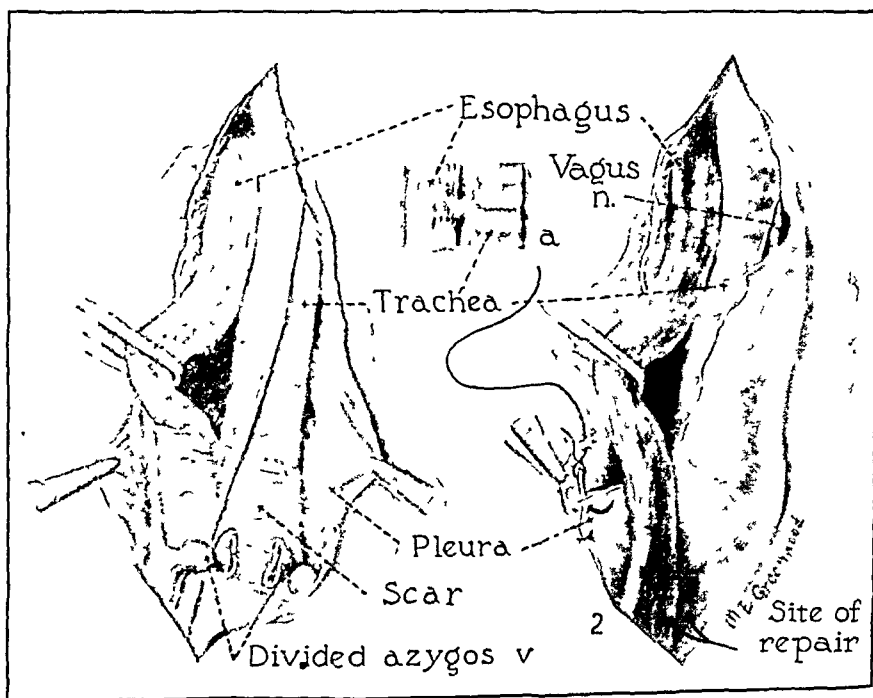
Cause	Number of Cases
Congenital.....	222
Mixed congenital.....	3
Neoplastic.....	367
Infectious (nonspecific).....	1
Infectious (specific).....	40
Syphilis.....	24
Tuberculosis.....	14
Actinomycosis.....	2
Traumatic.....	40
External foreign bodies (gunshot wounds).....	5
Internal foreign bodies (fishbones).....	22
Decubitis ulcer (in a case of substernal goiter).....	4
Operative.....	1
Following rupture of aneurysm.....	5
Following esophageal stenosis.....	3
Undetermined cause.....	2
Cause not specified.....	7
Total.....	682

patient was becoming less tolerant of the nasal tube, and, despite calculated adequate food intake, he lost 24 pounds (10.9 Kg.) in twenty-one days. Therefore a gastrostomy was done on April 21, 1947. Thereafter his strength and state of mind improved considerably. However bronchoesophagoscopy on June 28, approximately three months after injury, revealed a 3 mm. slit about 24 to 27 cm. from the incisor teeth "with edges smooth and epithelized."

*Preoperative Status.*—Immediately before surgical repair of the fistula was undertaken, the patient was in good condition. His weight was 160 pounds (72.6 Kg.); the erythrocyte count was 4,120,000; the hemoglobin level was 13.5 Gm. (normal 15.6 Gm.—100 per cent), and the leukocyte count was 12,800. The total serum protein level was 7.0 Gm. per hundred cubic centimeters of whole blood. Repeated roentgen ray studies revealed the persisting communication between the esophagus and trachea in the vicinity of the bifurcation. Administration of penicillin, 20,000 units every three hours, was begun the day before operation.

*Surgical Repair.*—Three months and eleven days after injury, with use of intratracheal cyclopropane-ether anesthesia, the right side of the chest was opened by removing the fourth rib from its bed. The azygos vein was doubly ligated

and divided between ligatures. The esophagus and trachea above the level of the lesion were exposed by incision of the pleura, and the interval between the two structures was carefully developed downward to the site of pathologic change, marked by dense scar tissue. The fistulous tract was exposed and divided. It was more than 1 cm. in its long diameter and was completely epithelized. The defects in the trachea and esophagus were closed in two layers with fine continuous chromic surgical gut sutures. A flap of mediastinal pleura was turned and placed so that it separated the suture lines in the trachea and esophagus. The mediastinal pleura was not closed. Closed drainage of the thorax was provided by means of an intercostal catheter in the dependent portion of the lateral chest wall. The chest was closed with interrupted chromic surgical gut sutures. During and immediately after operation the patient received 1,500 cc of whole blood through cannulas in both ankle veins.



Surgical repair of tracheoesophageal fistula

*Postoperative Course.*—The patient was given oxygen by nasal tube. Continuous suction through the gastrostomy opening was established. Besides penicillin, sodium sulfathiazole was given in parenterally injected fluids. On the third postoperative day the intercostal catheter was not functioning. Roentgen examination showed collapse of the middle and lower lobes of the right lung and evidence of air under tension. The catheter was removed and a thoracentesis was done for removal of air. On the fourth postoperative day another catheter was reinserted into the thorax through a new site. On the seventh postoperative day culture of the drainage showed colon bacilli and some hemolytic streptococci.

In the following days the patient had a septic fever and was very toxic, and the catheter drainage was inadequate. On the twenty-second postoperative day a thoracostomy was done by removal of a section of the tenth rib in the posterior axillary line. Evidently the patient had been eating despite advice to the con-

trary, for at operation the pulp of an orange was removed from the pleural cavity. The skin margins of the wound were sutured to the thick pleura to prevent premature closure of the opening. With open drainage established, the patient's condition improved and the empyema cavity decreased in size. He became dissatisfied, however, and absconded from the hospital before further evaluation of his status could be made.

Six months later the patient was persuaded to return to the hospital, and he was admitted on March 24, 1948. Physical examination revealed a functioning gastrostomy opening. Temperature, pulse, respiration and blood pressure were within the range of normal. A roentgenogram of the chest showed obliteration of the right costophrenic sinus. A calcified plaque was present in the same area. Results of routine laboratory studies were normal. Two days after admission the gastrostomy opening was closed under cyclopropane-ether anesthesia. The patient had a mild infection of the wound but was well enough to leave the hospital on his fifteenth postoperative day.

#### COMMENT

The present case presents several interesting features, the first of which is that tracheoesophageal fistula may occur from blunt violence, without demonstrable injury to the thoracic cage and without emphysema. In this case and in 2 other similar cases, previously mentioned and abstracted at the end of this article, the fistulas occurred in the region of intimate contact between the trachea and the esophagus, in the vicinity of the tracheal bifurcation.

Mediastinitis and early death were probably averted by early use of penicillin along with chemotherapy. Withholding of all oral intake and substituting feeding by the Levin tube and, later feedings through the gastrostomy opening were necessary adjuncts in the prevention of mediastinal infection as well as in building up the patient for reparative surgical procedures. It seems to us that feeding through an early gastrostomy opening is preferable to continued feeding by Levin tube.

While conclusions regarding the most satisfactory method of handling this type of case are not justified, it seems that surgical division of the tract is indicated as soon as the inflammation at the site of injury has subsided. The interposition of a flap of mediastinal pleura between the sites of repair of the two structures is recommended to lessen the chances of recurrence.

In connection with definitive treatment of tracheoesophageal fistula generally, it should be added that cases of successful closure of certain types of fistulas by endoscopic treatment of the area with caustics have been reported.<sup>2</sup> Spontaneous closure has also been reported.<sup>3</sup>

After surgical closure of the fistula has been accomplished, it is necessary to withhold food and drink by mouth until complete healing

2. Abbott, O. A.: *J. Thoracic Surg.* **14**:382 (Oct.) 1945. Clerf, L. H.: *Ann. Otol. Rhin. & Laryng.* **42**:920 (Sept.) 1933.

3. Rucks, W. L.: *Memphis M. J.* **7**:209 (Nov.) 1930.



has occurred. The surreptitious taking of food by the patient in the present case led to breakdown of the esophageal repair with consequent development of empyema, resulting from the collection of food material in the pleural cavity. It is remarkable how drainage of the empyema and the following expansion of the lung were effective in bringing about closure of the esophagopleural communication.

#### SUMMARY AND CONCLUSIONS

On the basis of this study, the following points appear to us to be of utmost importance as requisites for successful management.

1. Tracheoesophageal fistula occurring near the bifurcation of the trachea may result from steering wheel injuries. There may be no injury to the chest wall, nor need there be emphysema or severe shock.

2. The diagnosis should be considered whenever the patient has fits of coughing on taking food or drink. Confirmation is obtained by esophagoscopy and bronchoscopy together with roentgen study of the chest following ingestion of radiopaque material.

3. Chemotherapy and antibiotics aid in preventing infection.

4. Oral feeding is contraindicated.

5. Gastrostomy should be done as soon as practicable. In this case it was not done until three weeks of feeding by Levin tube had proved unsatisfactory.

6. The fistula is repaired through a right thoracotomy. Interposition of a flap of mediastinal pleura between the sites of repair is probably useful in preventing recurrence.

7. Underwater drainage of the thorax is recommended.

8. Postoperatively oral intake should be withheld until healing has been assured.

#### ABSTRACTS OF SIMILAR CASES FROM THE LITERATURE

1. Piquet, Muller, Marchand and Decoulx<sup>4</sup> report the case of a 31 year old man who was crushed against a wall by a machine and sustained fractures of the left third to fifth ribs at the "level of their anterior arcs" and fracture of the mandible. On the third day after injury, coughing occurred on attempts to take food or drink. The patient eventually learned to bend to the left when eating or drinking and in this manner abolished the associated spasms of coughing. Fluoroscopically, about one month later, ingested barium sulfate solution was seen to fill the right lower bronchus, establishing the presence of a broncho-esophageal fistula in the region of the bifurcation of the trachea. Broncho-esophagoscopy five months after injury revealed much scarring in the esophagus and in the right main bronchus. Roentgen examination several days later again revealed the fistula, which was not actually seen by endoscopy. The authors

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4. Piquet; Muller; Marchand, and Decoulx: *Ann. méd. lég.* **19**:125 (Feb.) 1939.

expressed the opinion that the fistula resulted from trauma, which probably brought about the rupture into the trachea of a preexisting traction diverticulum of the esophagus. The possibility of an asymptomatic congenital fistula as a basis for development of the fistula after trauma is dismissed by the authors as very unlikely, since very few instances of asymptomatic congenital fistulas have been observed. The treatment and eventual outcome are not reported.

2. Adams and Mabley<sup>5</sup> report the case of a 19 year old youth who was struck on the chest by a 700 pound (318 Kg.) box which had fallen 10 feet (3 M.). The patient had emphysema of the neck and face but not of the chest wall. He was in shock and presented evidence of laryngeal obstruction which necessitated tracheotomy. A Levin tube was passed into the stomach but did not prove satisfactory, and a gastrostomy was done. Thereafter the patient improved rapidly. Bronchoesophagoscopy revealed a large tracheoesophageal fistula just above the level of the carina. Approximately four months after the injury, the fistula was excised and the defects in the trachea and esophagus were closed. The chest was closed without drainage. Penicillin was given before and after operation. The postoperative course was uneventful, and on the fourteenth postoperative day the patient was able to eat a normal diet and to be up. In this case, despite the severe trauma, fracture of ribs, sternum or cartilages could not be demonstrated.

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5. Adams, H. D., and Mabley R. E.: *J. Thoracic Surg.* **15**:290 (Aug.) 1946.

# AN EXTRAVESICAL METHOD FOR THE RELIEF OF VESICAL OCCLUSION

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**M**R. TERENCE MILLIN'S method of extravesical prostatectomy has proved its merit clinically in the past three years. The retropubic approach is fundamentally not a new procedure, but Mr. Millin has developed it as a simple and successful method. We will discuss briefly the technic,<sup>1</sup> will recount our experience with retropubic prostatectomy<sup>2</sup> and will report the application of the retropubic approach in the treatment of obstructions of the vesical neck in infants and children.

The retropubic prostatectomy employs extravesical approach to the prostate gland, which is, though seemingly infrequently appreciated, an extravesical structure. In other words, by this approach one does not go through the bladder to attack a pathologic condition that lies outside the bladder, as is commonly practiced in the popular Freyer, or suprapubic, method.

The prostate is exposed through either a longitudinal or a transverse suprapubic incision which includes both skin and fascia of the rectus muscles. The rectus muscles are separated, the hypogastric fascia opened

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From the Department of Surgery, Division of Urology, University of Louisville School of Medicine.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Millin, T.: Retropubic Prostatectomy, *Lancet* **2**:693-696, 1945; Retropubic Prostatectomy, *J. Urol.* **59**:267-280, 1948; Retropubic Urinary Surgery, Baltimore, Williams & Wilkins Company, 1947. Grant, O.; Lich, R., Jr., and Maurer, J.: Retropubic Prostatectomy, *Urol. & Cutan. Rev.* **52**:9-12, 1948. Bacon, S. K.: Retropubic Prostatectomy, an Extravesical Technic, *J. Urol.* **59**:376-384, 1948.

2. Lich, R., Jr.; Grant, O., and Maurer, J. E.: Extravesical Prostatectomy: A Comparison of Retropubic and Perineal Prostatectomy, *J. Urol.* to be published. Grant, O., and Lich, R., Jr.: Rationale and Results in Retropubic Prostatectomy, *Ann. Surg.* **127**:1010-1021, 1948. Lich, R., Jr., and Maurer, J. E.: Retropubic Surgery, Kentucky M. J., to be published.

and the empty bladder displaced posteriorly and cephalad. The fat pad over the prostate is displaced laterally to expose the variable vascular endopelvic fascia overlying the prostate. If the veins are prominent, they are individually doubly ligated and severed. If the endopelvic veins are not large, they are disregarded and dealt with individually when bleeding ensues after incision of the prostatic capsule. It has been our practice to introduce a subcapsular suture at the apex of the gland, coursing through the anterior surface of the capsule, to diminish bleeding from the capsular veins. We think that this step is a valuable adjunct.

The prostatic capsule is incised transversely approximately 1.5 cm. distal to the vesicoprostatic junction. The length of the incision is dependent on the size of the prostatic adenoma and is great enough to facilitate an atraumatic enucleation. All layers of the capsule are divided with a single stroke of the knife, and the bulging adenoma can be seen in the opening of the capsular wound. Bleeding from capsular veins at this point may be brisk, but adequate visualization is easily provided by the use of suction. The individual veins are clamped and sutured for positive hemostasis. Mr. Millin employs electrocoagulation for bleeding vessels; however, we have not experienced similarly satisfactory hemostasis. It is to be recalled that these prostatic channels are large caliber veins which have a sparsity of muscle fiber. This may defeat the usual effectiveness of electrocoagulation.

After capsular hemostasis has been accomplished, the prostatic adenoma is separated from the false capsule with scissors point dissection throughout its entire anterolateral circumference, and before the gland is delivered into the retropubic space the posterior urethra is severed with scissors at the apex of the adenoma. When the gland is delivered from the capsule, it is elevated as much as possible in order to visualize its attachment to the vesical neck. The prostate is now attached to the bladder by only a mucosal cuff, and this is cut across. The adenoma is removed, and one can, for the first time, get a glimpse of the bladder cavity through the vesical neck. This entire procedure has been extravesical in both the approach and the enucleation of the adenoma.

The prostatic arteries at the prostatovesical junction are sought and ligated with a figure of eight suture. These arteries normally enter the prostatic capsule at its junction with the bladder at the positions of 5 and 7 o'clock. The vesical neck is then inspected for small bleeding vessels, which are lightly fulgurated. After the vesical neck is free of bleeding points, a catheter is introduced through the urethra; it traverses the prostatic fossa and enters the bladder through the vesical neck.

After the catheter has been introduced, the prostatic capsule is closed with a continuous suture of no. 1 chromic surgical gut including

all layers of the capsule. This suture must be started and terminated well beyond the angles of the capsular wound in order to control all postoperative capsular ooze.

A small drain is left in the space of Retzius; the abdominal wound is closed in layers, and the skin is approximated. Vesical drainage is accomplished by use of the urethral catheter alone. A bilateral vasectomy is done to prevent postoperative epididymitis.

The wound drain is removed on the second postoperative day, and the urethral catheter is removed on the fourth day after operation. The urine will usually be completely clear in twelve to eighteen hours.

We have tabulated herewith a résumé of our first 221 cases of retropubic prostatectomy, which are compared with 500 cases of other open surgical methods of prostatectomy, the majority of which were perineal prostatectomies performed by the late Dr. Owsley Grant

TABLE 1.—*Comparison of Results of Retropubic Prostatectomy and Open Surgical Prostatectomies*

Procedure	No. of Cases	Average Age, Yr.	Hospital Period		Catheter Period, Days	Mortality, %
			Total, Days	Post-operative, Days		
Retropubic prostatectomy.....	221	68.3	17.1	13.1	6.2	3.2
Open surgical prostatectomies.....	500	67.1	31.0	21.8	11.6	3.9

(table 1). It can be seen at a glance that the results are comparable, as might well be expected, since both procedures are extravesical methods of prostatectomy. It is to be noted further that some of the apparent improved figures in the retropubic group could well be occasioned by the fact that antibiotics and sulfonamides were available.

The mortality of 3.2 per cent in the retropubic group was accounted for by 7 patients, all of whom died within fourteen days postoperatively. One died on the fifth day of acute coronary thrombosis; another, 78 years of age, had an uncontrollable cardiac decompensation and bronchopneumonia and died in cardiac failure on the thirteenth day after operation. A man of 66 years died of an overwhelming perivesical infection which had presumably been present, though undiagnosed, preoperatively. He is considered as an ill chosen subject for prostatectomy. The patient would not tolerate either urethral or cystotomy drainage, since both had been used in an attempt to avert operation. The remaining four patients, of 71, 69, 77 and 59 years, died on the seventh, eleventh, thirteenth and sixth days postoperatively of bronchopneumonia, cardiac failure, uremia and an infarct, respectively. The surgical complications which prolonged hospitalization in the series of retropubic prostatectomies are noted in table 2.

Suprapubic fistula occurred in 2 patients. The first had severe diabetes and presented an infection of the wound and a most difficult problem in wound healing; the duration of the fistula was twenty-one days. The subsequent course of the patient has been excellent. The other patient had a huge, narrow-mouthed diverticulum which could not be resected because of the patient's generally poor state. The fistula healed on the twenty-seventh postoperative day.

Infection of the wound was recorded in any case in which there was induration of the wound and possibly some drainage causing the patient to be maintained in the hospital beyond the usually anticipated day of discharge. The longest period of hospitalization in this group was eighteen days.

Secondary hemorrhage from the prostatic bed occurred in 4 patients. In 2 of the group this condition developed during the period of hospitalization, and it was thought that the hemorrhage was due to bleeding from

TABLE 2.—*Surgical Complications*

Complication	No. of Cases	Incidence, %
Suprapubic fistula, temporary.....	2	0.9
Wound infection .....	11	4.9
Secondary hemorrhage from the prostatic bed.....	4	1.8
Osteitis pubis .....	2	0.9

the prostatic arteries, which had not been ligated. In both instances the bleeding was controlled by endoscopic methods employing electrocoagulation. In the remaining 2 patients the hemorrhages developed after the seventh postoperative day and were controlled by electrofulguration cystoscopically and a Foley catheter. Secondary hemorrhage from the prostatic bed is a hazard of prostatectomy from which no method described thus far has been immune.

There were 2 instances of osteitis pubis, both of which continued for approximately six months. One occurred in a hugely obese diabetic patient, whose convalescence was delayed by poor healing of the wound. The other patient's convalescence was uneventful until the third week postoperatively. From statements in the literature regarding this operation, the appearance of osteitis pubis seems to have been all too frequent, and this fact constitutes certainly a most valid criticism of the operation. It is to be remembered, however, that the syndrome may well not have been so clearly recognized in the past and many instances may have gone undiagnosed, and thus unreported, after other methods of prostatectomy. We have seen 1 instance following perineal prosta-

tectomy, and recently Rosenberg and Vest<sup>3</sup> reported 2 instances following transurethral resection.

We have used this surgical route to deal with lesions of the vesical neck and posterior urethra in infants and children. These lesions in the past have been approached either transvesically or transurethrally, and neither method has proved entirely satisfactory in our hands. The transvesical approach characteristically lacks adequate visualization and positive hemostasis in case of lesions of the vesical neck. The transurethral approach has certainly imposed mechanical limitations, particularly in infants. We are aware of the apparent satisfactory use of these two approaches in some clinics, but our experience has not been entirely without dissatisfaction.

We approach the prostate gland in precisely the same manner as the adenoma is approached, but instead of using a transverse capsular incision, we employ a longitudinal incision which extends from the apex of the gland to the prostatovesical junction. At the superior angle of the incision the lateral branches of the prostatic venous plexus are divided, and these vessels are ligated with a single suture on each side of the incision. These sutures are left long to act as tractors, and when lateral tension is exerted the entire posterior urethra and vesical neck are adequately exposed for visualization and palpation. We mention palpation particularly, since in 2 instances in which the obstruction of the vesical neck appeared visually to be relieved, we palpated some dense underlying tissue. This was removed, and the vesical neck could then be visualized and shown by palpation to be free of any obstructing tissue.

After removal of the tissue about the vesical neck, the bleeding points which occur at approximately 5 and 7 o'clock are ligated with a suture of fine surgical gut and immediately the wound is dry. The prostatic capsule is approximated with a running suture of fine chromic surgical gut after a catheter of small caliber has been introduced into the bladder per urethram. The abdominal wound is closed in layers, and a drain is left in place for two days. The catheter is removed on the fourth day, and voiding in these children is spontaneous and uncomplicated.

We have now treated 4 such children, from 3 months to 9 years of age, with excellent results. When the upper urinary tract was uninfected preoperatively, the urine was free of any cellular elements within eighteen days postoperatively. In only 1 case, that of a 3 month old child, did a suprapubic fistula occur, and it closed spontaneously after the catheter was reinserted for a four day period. We have followed 1 of these children for more than a year postoperatively and

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3. Rosenberg, M. L., and Vest, S. A.: *Osteitis Pubis*, *J. Urol.* **60**:767-775, 1948.

another for a six month period; the remaining 2 have been observed three and two months respectively. When an elevated nonprotein nitrogen level was stabilized preoperatively by catheter drainage, the level obtained did not change after operation. Morbidity has been surprisingly insignificant.

It can be seen from the statements that Mr. Millin's rediscovery of the retropubic, or anterior extravesical, approach to the prostate offers more than just another means of prostatectomy.

#### SUMMARY

The retropubic, or anterior extravesical, approach to the prostate gland is discussed and a series of 221 cases presented in which this method of prostatectomy was used to remove a benign prostatic hyperplasia. In addition, the value of this route in treating lesions of the vesical neck and urethra in infants and children is pointed out. A series of 4 cases is presented which demonstrated a most gratifying result in every instance. We report on this numerically inadequate group of children to suggest additional trial by others in an attempt to secure accurate evaluation. The real contribution is that for the first time a simple, effective extravesical approach to the prostate has been demonstrated which affords the simplicity of the suprapubic prostatectomy but, in contrast, is firmly established on sound surgical principles.



## SURGICAL MANAGEMENT OF RESPIRATORY EMERGENCIES DURING THE FIRST FEW WEEKS OF LIFE

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SINCE respiratory embarrassment in the newborn is a frequently encountered condition which may merit consideration and treatment from a surgical standpoint, it is our purpose to discuss 3 illustrative instances in which radical surgical measures were necessary in the treatment of infants whose dyspnea and cyanosis noted at birth failed to improve. Mitchell-Nelson's Textbook of Pediatrics<sup>1</sup> states that almost one half of the deaths of newborn infants are due to respiratory failure.

Morgan and Brown<sup>2</sup> listed nine accidents during labor which produced cyanosis of the newborn. Only one of these, aspiration of amniotic fluid, directly concerns the surgeon. This aspiration may cause bronchial obstruction with attendant emphysema or atelectasis, for which surgical treatment may be necessary. Since atelectasis is always present at birth, the degree and rate of expansion of the lungs in the newly born child may be significant.

Wasson<sup>3</sup> made roentgenograms of the chest at frequent intervals after birth to determine the natural history of aeration in the lung of the newborn infant. He found that in some infants whose delivery was easy the lungs were completely expanded in five minutes. After more prolonged deliveries, complete expansion of the lungs was noted at longer intervals after birth, in some cases being delayed up to two weeks. In some instances, entire lobes remained atelectatic; in others there were scattered areas of lobular atelectasis. The lower lobes were

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From the Department of Surgery of the University of Buffalo School of Medicine and the Children's Hospital.

1. Nelson, W. E.: Textbook of Pediatrics, Philadelphia, W. B. Saunders Company, 1946, p. 235.

2. Morgan, E. A., and Brown, A.: Cyanosis of the New-Born, J. A. M. A. **105**:1085 (Oct. 5) 1935.

3. Wasson, W. W.: A Roentgenographic Study of the Infant Chest As Seen at Birth, J. A. M. A. **83**:1240 (Oct. 18) 1924.

usually the last to expand. Clinical symptoms were or were not present, depending on the degree of atelectasis. It is important to keep the natal history in mind when considering a case of respiratory distress with signs and symptoms of pulmonary atelectasis.

Central disturbances caused by intracranial lesions with consequent poor pulmonary ventilation must be considered in cyanosis of the newborn. The premature infant may have marked underdevelopment of the bronchial tree as well as the thorax, which is evidenced by areas of the lung which do not become filled with air. Even agenesis of an entire lung has been reported.

Congenital diaphragmatic hernia is a cause of respiratory distress due to increased pressure on the lungs and mediastinum. This condition, which necessitates immediate surgical intervention in the newborn, has been relatively frequent in our experience and is not reported in detail. The subject has been adequately covered by other authors: Harrington,<sup>4</sup> Ladd,<sup>5</sup> Gross<sup>6</sup> and Donovan.<sup>7</sup> We are strongly of the opinion that reduction of the hernia and early repair of the defect are extremely important and prefer to operate on these infants within the first forty-eight hours of life, unless contraindications present themselves. For the same reason, tracheoesophageal fistula is not discussed but is included as one of the surgical emergencies encountered in dealing with the respiratory system. Eventration of the diaphragm has been reported and deserves a place in these considerations.<sup>8</sup>

Since overdistention of a lobe or lobes combined with mediastinal displacement during the first few weeks of life can cause what constitutes a surgical emergency, it is our desire to review the recorded cases and report in more or less detail the successful results and to discuss briefly the underlying conditions.

CASE 1.—A white boy, aged 11 weeks, was admitted to Children's Hospital Dec. 23, 1947. The birth history, obtained from another hospital (which is outside Buffalo), reveals an extremely difficult delivery, after which the child showed bruises over almost his entire body and one eye was closed from ecchymosis. The onset of breathing was slow, and mechanical resuscitation was necessary. Penicillin was administered because of elevation of temperature to 101 F. When the child

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4. Harrington, S. W.: Surgical Treatment of the More Common Types of Diaphragmatic Hernia; Esophageal Hiatus, Traumatic, Pleuroperitoneal Hiatus, Congenital Absence and Foramen of Morgagni: Report of Four Hundred and Four Cases, *Ann. Surg.* **122**:546, 1945.

5. Ladd, W. E., and Gross, R. E.: Congenital Diaphragmatic Hernia, *New England J. Med.* **223**:917, 1940.

6. Gross, R. E.: Congenital Hernia of the Diaphragm, *Am. J. Dis. Child.* **71**:579, 1946.

7. Donovan, E. J.: Congenital Diaphragmatic Hernia, *Ann. Surg.* **108**:374, 1938.

8. Bisgard, J. D.: Congenital Eventration of the Diaphragm, *J. Thoracic Surg.* **16**:484, 1947.

was taken home from the hospital after delivery, he appeared normal with the exception that he breathed with difficulty and retracted both ribs and abdomen with each respiratory effort. Six weeks after birth, a wheeze developed, which continued and became progressively worse. Approximately during the seventh week, he suffered an acute episode, at which time there was severe respiratory difficulty with profuse sweats and the infant seemed to gasp for air. The parents thought that he was dying. After medical treatment administered by the local physician, the wheeze disappeared, only to return again. There was only an insignificant cough and no cyanosis. On the day before admission, he had more trouble breathing. On admission, the child was in considerable distress; respirations were labored, wheezy and associated with substernal retraction. He was not cyanotic but assumed a dusky hue when he cried.

Physical examination revealed nothing of significance except for the thorax. There were rapid wheezing respirations with both phases shortened. Substernal retraction was noted. There was very little expansion of the thoracic cage. Breath sounds were decreased throughout the entire left side of the chest and increased in the lower right pulmonary field; they were diminished in the right upper field. Posteriorly, rales were heard at the apex of the right lung. Percussion revealed hyperresonance at the base and dullness at the apex of the right lung. Findings were unchanged over the left side. The cardiac dullness was detected in the right side of the chest. The tones were distant and not well heard. They were most distinct between the right midclavicular line and the sternum in the fourth interspace. The child was afebrile, with respirations averaging 32 per minute. He was in oxygen much of the time preoperatively and showed evidence of slight cyanosis when crying or moving about. His appearance was listless, and his feedings were taken poorly. Determinations of the hemoglobin level showed an average value of 12 Gm., and the white blood cells ranged from 6,550 to 18,400 preoperatively, with 46 per cent filamented cells, 8 per cent band cells, 42 per cent lymphocytes and 4 per cent eosinophils. Otherwise, the results of laboratory studies were of no significance. Bronchoscopic examination was done on December 26. A 3.5 mm. bronchoscope was easily passed. The trachea, both main bronchi and the carina were normal. There was no evidence of inflammation. A thin white mucus was seen, which was cultured. A growth was obtained which was reported as a gram-negative bacillus identified as *Escherichia coli*. The orifice of the right main bronchus could be seen, and it appeared normal. The orifice of the bronchus to the upper lobe of the left lung could not be seen because there was a slight bulge at this area. An impression was gained that mucosa was everted at the opening of the upper lobe. It was felt that this could be compatible with a distended upper lobe and that if any obstruction in the bronchus to the upper lobe of the left lung was present it was beyond the point of visualization.

*Operation (L. J. L.).*—When the infant was 14 weeks of age, under intratracheal anesthesia administered through a no. 1 Magill tube, a posterolateral incision was made over the left side of the chest. The thorax was opened through the fifth interspace, and on opening of the pleura the lung bulged through the incision, without positive pressure applied by the anesthetist. On examination of the left side of the thorax, a large mediastinal hernia, a greatly overdistended upper lobe and a collapsed lower lobe were observed. The upper lobe occupied practically the entire side, and the lower lobe was merely a small, shrunken mass against the mediastinum. The upper lobe was pink; the pleural surface was tense and smooth. It appeared to be definitely emphysematous throughout. It was impressive to note that the vessels to the upper lobe were smaller and more collapsed than normal. The lobe did not deflate after removal. There were no



Fig. 1 (case 1).—Preoperative and postoperative roentgenograms of an infant with hypertrophic emphysema.



Fig. 2 (case 1).—Resected upper lobe of left lung, showing marked distention.

cystic areas visible. The upper lobe was removed after individual ligation of the vessels with silk. The bronchus was amputated close to its origin, about 0.5 cm. beyond its division from the main bronchus, and the stump was closed over with interrupted silk sutures. Moderate positive pressure was applied through the intratracheal tube, and there was no leakage of air from the bronchial stump. The lower lobe seemed to aerate without any difficulty. A no. 12 F. de Pezzar catheter was placed in the posterior portion of the wound, which was closed in layers with chromic surgical gut. Fluids and whole blood were introduced through a cutdown in the ankle vein during the operation.

The postoperative period was without untoward incidents. Feedings were resumed on the afternoon of operation and continued without interruption. Administration of oxygen was maintained for twenty-four hours and was not necessary thereafter. The catheter was removed from the thorax at the end of thirty hours, with a total drainage of 220 cc. of clear, amber-colored fluid. A roentgenogram taken with a portable machine on the afternoon of operation showed the lower lobe of the left lung to be reexpanded. The mediastinum was central, and there was an area of density in the upper half of the left side of the chest. The right lung was aerated in all lobes.

*Pathologic Report.*—Various sections taken from the extirpated lobe showed largely alveolar emphysema with some blebs of considerable size, exceeding that of the lumens of all bronchi contained in this section. Although some of the bronchi were dilated, their lumens were free of secretion. There was some edema surrounding the pulmonary arteries in the hilar area, extending through the interlobular fissures into the pleura. Numerous distended air sacs alternated with distinctly atelectatic areas. Some intervening lobules contained very thin watery material (edema) with but few desquamated macrophages. Some smaller caliber bronchi draining the atelectatic areas were also completely collapsed.

Other sections showed a largely similar picture, with prominently distended bronchi, air sacs and alveoli and with some edema intervening between the alveoli which were not atelectatic. In other sections, again taken from the perihilar area, the atelectasis was considerable with the bronchi entirely collapsed, while nearby bronchi, only a few millimeters away, as well as part of the adjacent alveolar tissue appeared markedly distended. Part of the subpleural lobules, however, appeared entirely collapsed. In this section edema, involving again the interlobular fissures, was pronounced. The elastic membranes in the arteries and bronchi throughout were well preserved.

Finally, in several lobules near the hilus the atelectatic alveoli were almost entirely filled with the previously mentioned debris containing macrophages but no other cellular exudate. The pulmonary arteries surrounding bronchi of first order at the hilus appeared very prominently separated from the partly atelectatic pulmonary tissues by periadventitial edema.

*Postoperative Course.*—Follow-up examination six months after operation revealed breath sounds normal throughout both sides of the chest and the heart in normal position. The parents stated that since discharge from the hospital the child had breathed easily at all times, there had been no struggle and, whereas prior to operation he used to "shake the crib with his efforts," respirations were now perfectly normal. There had been a steady gain in weight. Roentgen examination showed all the remaining lobes to be clear, well aerated and normal in position. The lower lobe of left lung had not completely filled the hemithorax but had progressively increased in size to occupy the position of the resected upper lobe. The weight was 23 pounds (10.4 Kg.).

A survey of the literature and textbooks on pathology fails to reveal a classification which exactly fits this particular type of lesion unless it is assumed that a bronchial obstruction existed in the upper lobe of the left lung.

Jackson<sup>9</sup> discussed thick secretions as the cause of bronchial obstruction. In our case there was no evidence of bronchiectasis or cystic disease. Royes,<sup>10</sup> in a case report on an adult, entitled "Localized Hypertrophic Emphysema," described emphysema of the middle lobe due to a flap of mucous membrane which included five eighths of the lumen of the bronchus. He assumed that this mucosal flap acted as a valve and gave rise to the localized hypertrophic emphysema. There were no cavernous areas found.

Gordon<sup>11</sup> referred to a flap of mucous membrane lodging in a bronchus in such a manner that a check valve mechanism occurred and discussed the mechanism of hypertrophic pulmonary emphysema. He mentioned that the condition is reputed to be without known cause but that there are a multitude of suggestive theories of origin, which he discussed and largely discredited as causative agents. None of them would in any way apply to the case herein reported unless it is assumed that the bronchial mucosa was redundant. Gordon retained two theories as having, in his opinion, some validity. These are (a) the theory of compensatory distention and (b) the theory of obstruction; he commented that the theory of obstruction is a subdivision of the theory of compensatory distention.

Caffey,<sup>12</sup> in a paper in which he discussed regional obstructive pulmonary emphysema in infants and children, reported 7 cases, in each of which there was associated respiratory infection. The youngest patient was 3 months of age. Cystic dilatation, which was universally noted on the roentgenograms of the chest, was explained on the basis of emphysema. The lesions were not thought to be consistent with pulmonary abscess or congenital cystic disease of the lungs. In all these patients the return to normal was observed following nonoperative treatment. This author stated that if the bronchial obstruction is of

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9. (a) Jackson, C.; Spencer, W. H., and Manges, W. F.: The Diagnosis and Localization of Non-Opaque Foreign Bodies in the Bronchi, *Am. J. Roentgenol.* **7**:277, 1920. (b) Jackson, C.: The Mechanism of Physical Signs with Especial Reference to Foreign Bodies in the Bronchi, *Am. J. M. Sc.* **165**:313, 1923. (c) Jackson, C.: Bronchoscopy: Past, Present and Future, *New England J. Med.* **199**:759, 1928.

10. Royes, K.: Localized Hypertrophic Emphysema, *Brit. M. J.* **2**:659, 1938.

11. Gordon, I.: The Mechanism of Hypertrophic Pulmonary Emphysema, *Dis. of Chest* **10**:180, 1944.

12. Caffey, J.: Regional Obstructive Emphysema in Infants and in Children. *Am. J. Dis. Child.* **60**:596, 1940.



Fig. 3 (case 1).—Photomicrographs of resected emphysematous lobe.

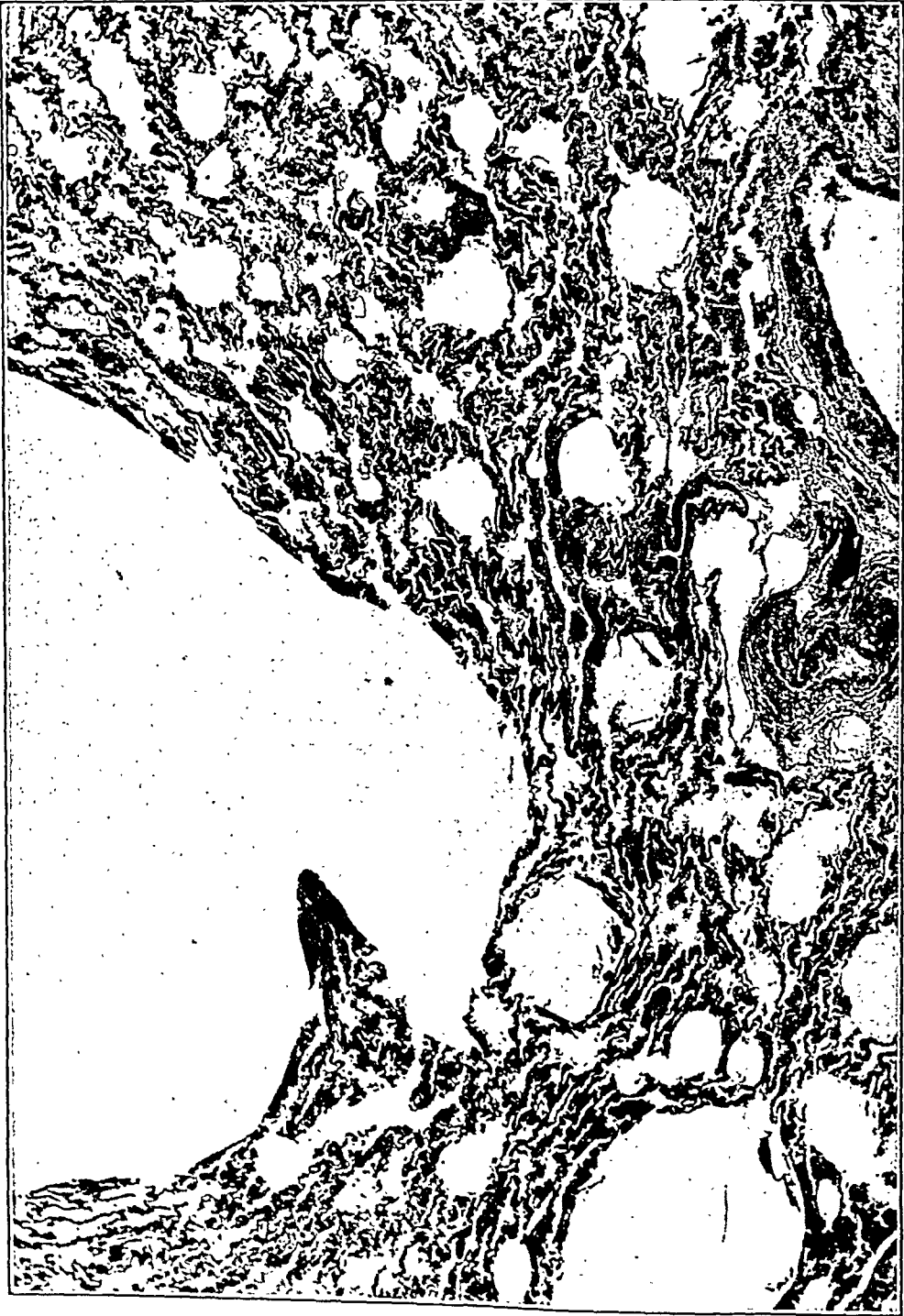


Figure 3 continued.



the check valve type, so that the inflow of air is free during inspiration, the escape during expiration is obstructed and accumulative alveolar distention occurs in the distal segment of the lung.

Paine<sup>13</sup> and others have shown experimentally that emphysematous changes followed placement of check valve obstructions in the trachea of dogs. Rubin,<sup>14</sup> in his textbook, mentioned that since the distended lungs are in contact with the chest wall forcible compression is required in an effort to deflate them in order to permit an interchange of gases and stated that all the accessory muscles of respiration have to be brought into action. This could explain the abnormal breathing that this infant exhibited.

Snow and Cassasa<sup>15</sup> reviewed roentgenograms of 70 infants under 1 year of age with a clinical diagnosis of pneumonia. It was their observation that in almost every case there was some degree of emphysema, with extreme degrees in many cases, particularly in infants under 6 months of age. Displacement and rotation of the heart with depression of the diaphragm was noted. They emphasized the point that severe tension was necessary for displacement of the mediastinum. These observers felt that the changes in aeration of the lung were caused by valvular effects in the bronchial tree which were the result of inflammatory reactions and secretions. Four roentgenograms reproduced in their article illustrate conditions closely similar to those in the case herein described.

McNeil and co-workers<sup>16</sup> stated in an article dealing with pneumonia in children that a degree of acute vesicular emphysema may be present in either lobar pneumonia or bronchopneumonia.

Maxwell<sup>17</sup> discussed the subject of localized emphysema from the standpoint of incomplete bronchial obstruction and reported 6 cases. One of the patients was a 2½ year old child whose left lung was in such a state of extreme emphysema that spontaneous pneumothorax was suspected. There was sudden change in physical signs before bronchoscopy could be accomplished, and within a few hours the clinical signs and symptoms returned to normal. This was confirmed by roentgenograms. Mucus was assumed to be the causative agent.

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13. Paine, J. R.: Studies in the Experimental Production of Pulmonary Emphysema, *J. Thoracic Surg.* **10**:150, 1940.

14. Rubin, M., and Rubin E.: *Diseases of the Chest*, Philadelphia, W. B. Saunders Company, 1947, p. 355.

15. Snow, W., and Cassasa, C. S.: Obstructive Emphysema and Atelectasis in Acute Respiratory Diseases of Infants, *Am. J. Roentgenol.* **37**:220, 1937.

16. McNeil, C.; McGregor, A. R., and Alexander, W. A.: Studies of Pneumonia in Childhood, *Arch. Dis Child.* **4**:83, 1929.

17. Maxwell, J.: Localized Emphysema As a Sign of Incomplete Bronchial Obstruction, *Brit. M. J.* **1**:520, 1940.

Salmon and Davenport<sup>18</sup> studied the autopsy findings in 6 infants who died shortly after birth with pneumothorax and pulmonary emphysema. There was no evidence of bronchial obstruction in these lungs. They examined the lung under the dissecting microscope and found a honeycomb appearance due to extensive interstitial pulmonary emphysema. Excessive pulmonary ventilation incident to difficult birth and artificial respiration caused rupture of the alveoli, in their opinion. The air liberated in this fashion dissects along the pulmonary vessels and on reaching the visceral pleura may rupture through and even cause a pneumothorax. The air remaining in the interstitial pulmonary tissues may cause a very inelastic lung which collapses but little during the respiratory cycle. The authors applied the general term "air block" to this condition, in which air reaches the interstitial pulmonary tissue and may spread to the pleural cavity, to the mediastinum, to the retro-peritoneal space and even over into the other lung. This affords a plausible explanation for extensive degrees of emphysema not associated with bronchial obstruction.

The etiologic factor in our case has not been determined. Bronchoscopic examination suggested some bulging in the location of the bronchus to the upper lobe. It is not clear whether this was obstructive in nature and whether the respiratory difficulties at the time of birth, which required rather energetic efforts to overcome, were significant. There was evidence of pulmonary infection both immediately after birth and at 7 weeks of age. Also a wheeze was noted by the parents. Examination at the time of operation failed to reveal any obstructive lesion, and careful dissection of the gross specimen and further microscopic investigation failed to show any obstructive type of lesion. Although evidence of bronchial obstruction was not positive, it was at least highly suggestive, but we are at a loss to discover the type or location. There was no evidence of pneumonia in the resected lobe. This infant was operated on with the probable diagnosis of cystic disease.

The next case, which followed a somewhat similar course, proved to have an extrapulmonary lesion as a causative factor. Immediate operation established the diagnosis and resulted in complete relief of symptoms.

CASE 2.—A. B., a white boy, was delivered normally at term and weighed 8 pounds (3,630 Gm.). Shortly after birth he was observed to have rapid, labored respirations and cyanosis. The child was placed in oxygen. Frequent suctioning of the pharynx was necessary to remove mucoid secretions. The temperature varied from 99.2 to 101.4 F.; respirations, from 80 to 110, and pulse rate, from 110 to 140. Examination of the chest revealed marked suppression of the breath

18. Salmon, G. W.; Forbes, G. B., and Davenport, H.: Air Block in the New Born Infant, *J. Pediat.* 30:260, 1947.

sounds on the right, with dulness to percussion throughout. The roentgenogram showed atelectasis of the upper and lower lobes of the right lung and emphysema of the middle lobe.

Bronchoscopy showed the right main bronchus to be nearly occluded in its lower portion by a swollen membrane and thick mucus. The mucus was removed and a dilating forceps introduced and expanded. Improvement of breathing followed. The child was able to be out of oxygen without cyanosis. The temperature returned to normal. The upper lobe expanded, and the middle lobe became less emphysematous, but the lower lobe remained atelectatic on roentgen examination. On the tenth day after birth the general condition seemed good, and the formula was being taken well; hence the child was discharged from the hospital.

Three weeks later, the child was readmitted because of cyanosis and labored breathing. The clinical impression was of a pleural effusion on the right side with mediastinal shift. This impression was confirmed by roentgen study. The temperature remained normal. On examination the blood and urine were normal. The child was again placed in oxygen.

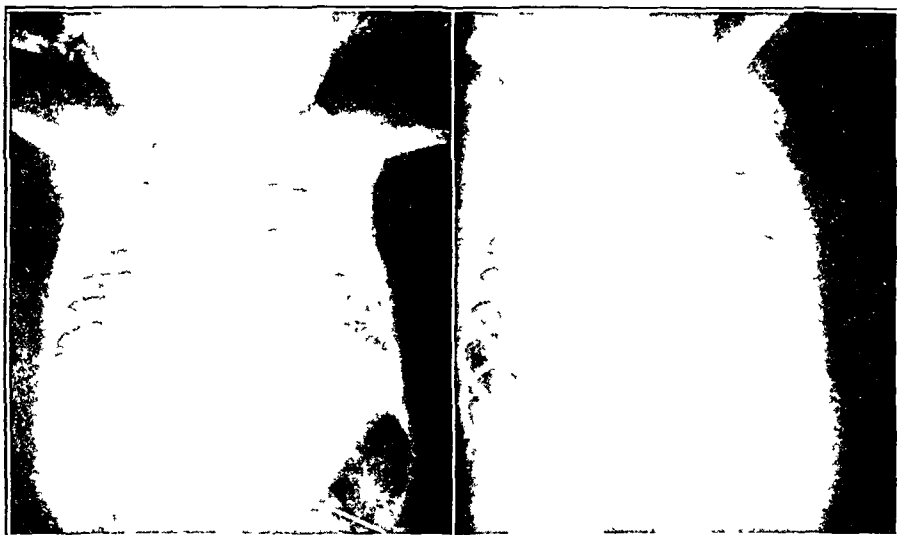


Fig. 4 (case 2).—Anteroposterior and lateral roentgenograms taken shortly after birth of an infant with gastrogenic cyst.

During the next two weeks, six thoracenteses were performed on the right posterior part of the chest, fluid varying from 30 to 80 cc being removed. This resulted in marked improvement in the child's condition. The fluid was clear and straw colored. It contained 350 to 500 polymorphonuclears, chiefly lymphocytes, per cubic centimeter. The total protein content varied from 0.6 to 0.7 Gm. per hundred cubic centimeters. No organisms were recovered on culture. Repeated roentgen examination of the child by now showed a marked change. The upper two thirds of the right side of the chest showed the presence of a small amount of air, with slight pleural thickening. A large pocket measuring 6 by 5 by 4 cm. with a wall 1 cm. thick was found in the lower posterior half of the right side of the thorax. This pocket had a fluid level.

A diagnosis of congenital pulmonary cyst was made, and the child operated on (W. L. B.) at the end of the seventh week of life, under cyclopropane anesthesia

administered through an endotracheal tube. The parietal pleura on the right was found to be thickened and dull in appearance. The visceral pleura, which was also thickened, was everywhere adherent with fibrinous adhesions which were easily separated bluntly. A small pocket containing shaggy fibrinous exudate and straw-colored fluid was found in the right costophrenic sinus. As they approached the posterior thoracic gutter, the two pleural layers were so densely adherent that they were not separated for fear of tearing the lung. At this point the dissection was begun in the retropleural space. A thick cyst wall was encountered, which was freed from the pleura anteriorly and the endothoracic fascia posteriorly. As the procedure developed, it became obvious that the wall was made up of smooth muscle, the appearance being exactly like that of stomach. An anomalous vessel the size of a match supplied it from the aorta, as did three branches from intercostal arteries. As the dissection progressed, the cyst was found to lie contiguous with the lower esophagus for a distance of 4 cm. and to send a projection to the cardia of the stomach. It measured 12 by 7 by 6 cm., and when it was opened

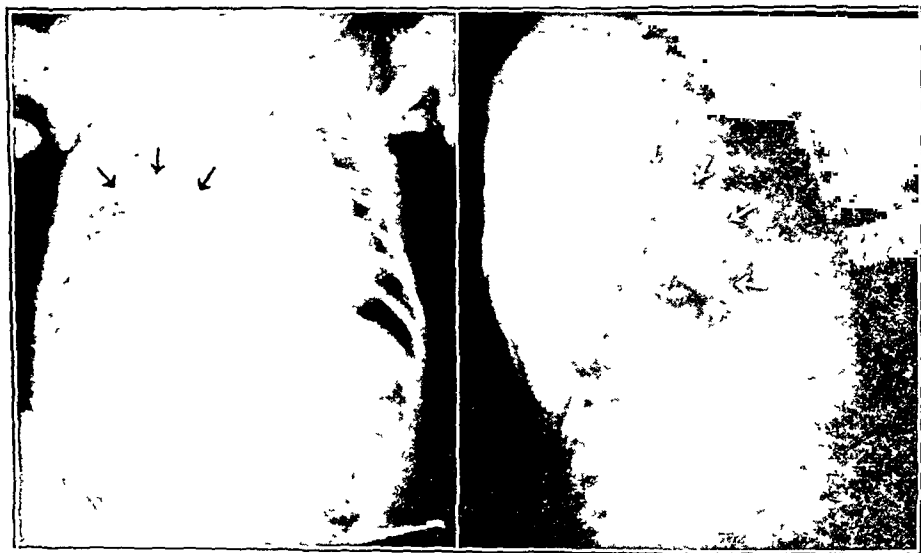


Fig. 5 (case 2).—Anteroposterior and lateral roentgenograms of infant with gastrogenic cyst taken immediately before operation.

typical gastric rugae were seen, together with clear fluid. The lung was reexpanded, and the thoracic cavity was closed without drainage. A roentgenogram taken at the conclusion of the operation showed the lung to be completely reexpanded.

The postoperative course was entirely uneventful. The child left the hospital two weeks later, in excellent condition, with all lobes of the lung reexpanded. Section of the cyst wall showed all layers—mucosa, submucosa and the outer muscular layers—to correspond exactly to layers of the normal stomach. One small tubelike projection showed a mucosa which resembled a jejunal pattern with well preserved villi. The histologic diagnosis was gastrogenic cyst.

This case was important because of its changing manifestations and the speculation that was aroused as to the exact cause of the respiratory distress. Roentgenograms taken shortly after birth revealed a homogeneous density over the right side of the chest that was inter-

pieted as atelectasis. Later films were suggestive of varying degrees of bronchial obstruction with atelectasis of the upper and lower lobes of the right lung, accompanied with emphysema of the middle lobe. Bronchoscopic examination did not reveal the cause of the obstruction, but the increased drainage which followed appeared to result in better aeration of the lung and improvement in the infant's condition. Again difficulty in breathing and cyanosis occurred. This time the roentgenogram suggested a pleural effusion. Thoracentesis apparently established this impression as true but was followed by a rapid reaccumulation of the fluid. The diagnosis was finally established on the basis of a roentgenogram taken after one of the aspirations of the chest. The fluid in the cyst cavity had probably been aspirated on this occasion,



Fig. 6 (case 2) —Resected gastrogenic cyst.

since the film showed a typical cyst structure. This was interpreted as being a pulmonary cyst. Thus the protean nature of the cyst prevented an exact diagnosis until the thoracotomy was done.

Intrathoracic cysts of gastric origin were formerly considered rarities. Now, with the increasing frequency and safety of surgical procedures within the thoracic cavity, reports are more numerous. A backward look over the literature will necessarily fail to give completely accurate information because of terminology. Many mediastinal cysts have linings which indicate their origin from multiple sources. Combinations of bronchial, esophageal, gastric and enteric types of mucosal linings are found. Cysts with a lining of gastric mucosa are usually larger and produce severe symptoms, as found in this case. Cysts of

esophageal origin tend to be smaller and are more compatible with life.

Olenik and Tendatnick<sup>19</sup> have reported a cyst of mixed gastric and intestinal epithelium in a 9 day old boy and have added an extensive survey of the literature up until 1947. They found 74 cases of intrathoracic cysts of foregut origin. In 27 of the collected cases the cysts were of gastric or intestinal origin. It is significant that the oldest of these 27 patients was aged 3 years and 9 months. This implies that these cysts exert an exceedingly dangerous influence on the child. Surgical consideration cannot fail to take this into account. Operative intervention was undertaken in 16 of these cases, with a successful outcome in 8.

Since that report, Davis and Salkin<sup>20</sup> have found 26 cases reported in the literature, with surgical treatment in 17, which was successful in 10. Adding the cases with successful outcome reported by these groups of authors to that of Lindquist and Wulff,<sup>21</sup> a case recently reported by Ehler<sup>22</sup> and the case here described, the total is 21 with 14 recoveries. Cases in older age groups are now being reported; Dickson, Clagett and McDonald<sup>23</sup> operated on a girl, aged 10; Davis and Salkin,<sup>20</sup> on a girl, aged 14, and Schwarz and Williams,<sup>24</sup> on a man, aged 23.

The symptoms of these cysts are those of pressure in the mediastinum. Cough, cyanosis, dyspnea and regurgitation of food result. More specifically, the pressure may be on the bronchus, in which case it is followed by atelectasis, obstructive emphysema and occasionally hemoptysis. If the child lives long enough, recurrent pneumonia and bronchiectasis occur. Hematemesis has resulted from pressure on the esophagus.<sup>25</sup> Peptic ulceration of the gastric cyst with penetration into the lung is a rare finding.<sup>26</sup>

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19. Olenik, J. L., and Tendatnick, J. W.: Congenital Mediastinal Cysts of Foregut Origin, *Am. J. Dis Child.* **71**:466, 1947.

20. Davis, E. W., and Salkin, D.: Intrathoracic Gastric Cysts, *J. A. M. A.* **135**:218, 1947.

21. Lindquist, N., and Wulff, H. B.: Mediastinal Enterocystoma, *J. Thoracic Surg.* **16**:468, 1947.

22. Ehler, A., and Atwell, S.: Gastric Cyst of the Mediastinum, *J. Thoracic Surg.* **17**:809, 1948.

23. Dickson, J. A.; Clagett, O. T., and MacDonald, J. R.: Intrathoracic Gastric Cyst, *J. Thoracic Surg.* **15**:318, 1946.

24. Schwarz, H., and Williams, C. S.: Thoracic Gastric Cysts, *J. Thoracic Surg.* **12**:117, 1943.

25. Ladd, W. F., and Scott, H. W.: Esophageal Duplication or Mediastinal Cysts of Enteric Origin, *Surgery* **16**:815, 1944.

26. Seydl, G. H.: Eine kongenitale Magenwandcyste im Mediastinalraum mit in die Lunge perforiertem Ulcus pepticum, *Frankfurt. Ztschr. f. Path.* **52**:346, 1938.

If the diagnosis can be made otherwise, we feel that aspiration of the cyst is dangerous, as it may lead to infection. Experience seems to point now to the fact that immediate excision of the cyst is the safest course to follow. As Ladd and Scott have pointed out, marsupialization may be necessary in certain cysts that have a muscular wall in common with the esophagus. Later these authors accomplish destruction of the lining of the cyst.

The third case again exemplifies an occasion of the futility of conservative efforts to overcome dyspnea and cyanosis when the underlying condition was congenital cystic disease of the lung.

CASE 3.—R. R., a white boy, was delivered normally at term. At first, he had some difficulty in breathing, but oxygen was not necessary. However, the mother

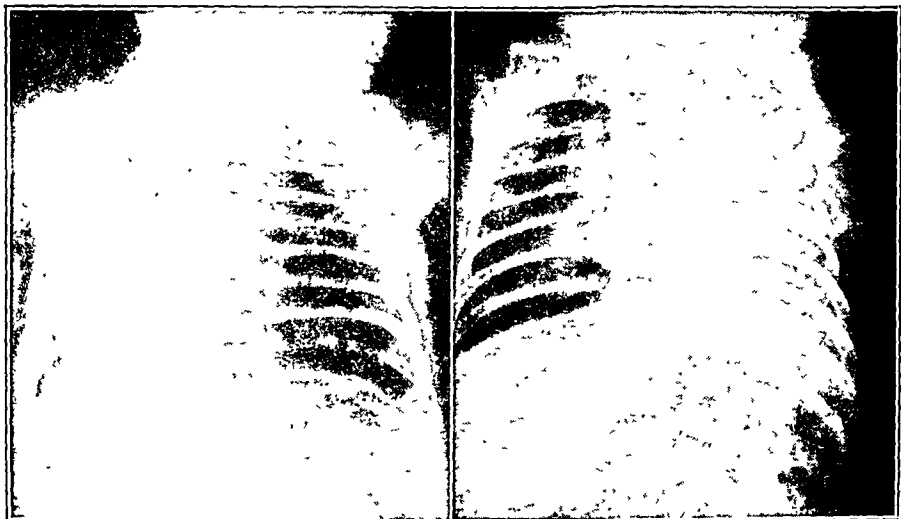


Fig. 7 (case 3).—Preoperative (anteroposterior) and postoperative (anteroposterior) roentgenograms of infant with cystic disease of the left lung.

stated that breathing had never been normal since birth, that the child cried in gasps and turned blue when crying hard. The child was so easily exhausted by any movement that it interfered even with his eating. There were three previous admissions to another hospital, where the child was given oxygen therapy for dyspnea. He was admitted to the Children's Hospital at the age of 7 weeks.

Roentgen examination showed marked emphysema of the entire left lung with large bleb formation, particularly at the base. The heart and mediastinum were shifted to the right. There was increased density of pulmonary tissue on the right consistent with compression atelectasis of the right lung.

Operation was carried out under cyclopropane anesthesia on the day of admission by Dr. J. F. MacManus. When the left pleural cavity was opened, the entire lung was found to contain numerous cysts, particularly the upper lobe, which had been completely replaced by large cysts. The air was removed from the large cysts to facilitate removal, and hilar dissection was carried out, with removal of

the lung. The bronchus was closed with interrupted silk sutures. The mediastinal pleura was closed with interrupted silk sutures and the chest closed without drainage.

The postoperative course was uneventful except for a mild unexplained febrile reaction which began on the sixth postoperative day and lasted three days. The child left the hospital at the end of two weeks in excellent condition and without any difficulty in breathing. The examination of the removed specimen showed the entire lung to contain multiple cysts varying in size from that of a match head to that of a walnut. Sections through the cysts showed a well preserved high columnar epithelial lining resting on a thin mesenchymal membrane attached to a thin layer of smooth musculature. The intervening pulmonary tissue showed pressure atelectasis.

The chief importance of pulmonary cysts relative to this discussion is the tendency of one type to cause a serious degree of respiratory distress. This is the expansile, or balloon, cyst. In Schenck's<sup>27</sup> series of cases collected from the literature, 86 per cent of expansile cysts were found in infants. These cysts are all connected with the bronchial tree, but when the connection is of a tortuous type air may be trapped within them, producing a great increase in size. This expanding lesion within the chest may cause severe displacements in the mediastinal organs as well as pulmonary compression. Cyanosis and rapid, tugging, inefficient respirations from the compression during the first few days or weeks of life demand immediate relief.

The type of relief decided on in the case reported here was pulmonary resection. Four previous instances<sup>28</sup> have come to our attention in which lobectomy or pneumonectomy was performed for this emergency in infants. The results have been uniformly good. Absence of infection and ease of developing the hilus in the infant contribute to the smoothness and speed of the operative procedure. The postoperative events in these reported cases and in our own case indicate that the infants withstand the operation remarkably well.

In 1933, Anspach and Wolman<sup>29</sup> reported a case of a large balloon cyst discovered in infancy and described 5 other cases collected from the literature. All the patients had died. They said that "surgical removal of lung cysts has not been attempted in infants. It is hoped that a

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27. Schenck, S. G.: Diagnosis of Congenital Cystic Disease of the Lung, *Arch. Int. Med.* **60**:1 (July) 1937.

28. Fischer, G. C.; Tropea, F., and Bailey, C. P.: Congenital Pulmonary Cysts, *J. Pediat.* **23**:219, 1943. Gross, R. E.: Congenital Cystic Lung, *Ann. Surg.* **123**:229, 1946. Burnell, W. E., and Caswell, H. T.: Lobectomy for Pulmonary Cysts in a Fifteen Day Old Infant with Recovery, *Surgery* **23**:84, 1948. Chisholm, T. C.: Lobectomy for Pulmonary Cysts in a Five Day Old Infant, personal communication to the authors.

29. Anspach, W. E., and Wolman, I. J.: Large Pulmonary Air Cysts of Infancy, *Surg. Gynec. & Obst.* **56**:635, 1933.



satisfactory treatment will eventually be devised to prevent high mortality in infants and young children." In their series of cases, repeated thoracentesis failed to prevent death from asphyxia. Even a tube with a one way valve placed into the cyst was unavailing. The use of thoracentesis may be associated with untoward results. Spontaneous pneumothorax with inability to expand the lung may follow. Even a tension pneumothorax can occur.

There is always the danger of infection and the grave results of toxemia from this source in infants. Collapse, necessitating the use of artificial respiration to maintain life, has resulted from thoracentesis. Numerous examples can be found in the literature in which aspiration of the cyst was followed by only momentary or no improvement, the infant dying a few days to weeks later.

In some instances the primitive bud from which the cyst has developed is so separated from the rest of the lung that the cyst alone can be removed by ligating its pedicle. We have encountered such a cyst in an adult. However, most of the time the enucleation of the cyst is not feasible in infants, as the separation of the cyst from the lung involves too much loss of blood. If the infant's condition is very poor on the operating table one can consider marsupialization of the cyst. This procedure leaves an avenue open for subsequent infection and necessitates further surgical measures. A tourniquet ligation of the hilus of the lung or the lobe could be considered if the risk is desperate. Although this is more easily accomplished and followed by better results in infants than in adults, individual ligation should be performed unless the circumstances are most extenuating.

Nonexpansile and fluid-filled cysts have not been discussed. They do not ordinarily constitute an emergency during the first few days of life. However, if they did, pulmonary resection would, in our opinion, provide the safest procedure.

The danger resulting from aspiration of these cysts must be emphasized. Aspiration may lead to infection or a leak in the cyst wall, causing tension pneumothorax. Either of these eventualities may seriously compromise the infant's chance to get well and cause serious complications. Immediate resection will carry a more favorable prognosis than any temporizing procedure. Souders<sup>30</sup> has commented on the well known propensity of these cysts to interfere with pulmonary function and give rise to recurring episodes of pulmonary infection by their pressure on a bronchus.

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30. Souders, C. R.: The Sequelae of a Balloon Cyst, *Lahey Clin. Bull.* 5:249, 1948.

## CONCLUSION

It appears that immediate removal of the underlying pathologic cause is the safest measure to relieve the respiratory embarrassment in the types of cases reported.

We feel that nothing is to be gained by delay, since progression of the tension within the lesion and infection are a constant threat to the child's life.

Aspiration of intrathoracic cystic lesions in infants increases the danger from infection or tension pneumothorax.

ADDENDUM.—Since this report was submitted for publication, we have encountered an instance of severe dyspnea in a newborn infant, caused by eventration of the left half of the diaphragm. This was repaired by a transabdominal approach, with reposition of the diaphragm at its normal level and complete clinical recovery.

Dr. Kornel Terplan, pathologist to the Children's Hospital, made the histologic examinations of the tissue in these cases.

## SURGICAL MANAGEMENT OF OMPHALOCELE

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**A**N OMPHALOCELE is a congenital anomaly that is occasionally seen. Some authors<sup>1</sup> have estimated the incidence as being 1 in 5,000 births. This ratio means, in itself, that the presence of a true omphalocele is a relatively rare surgical condition. It is probably true that up until the past several decades a number of infants with omphaloceles were allowed to die without surgical intervention or, if an attempt were directed toward surgical correction, it was unsuccessful and the termination was fatal. Even though the number of omphaloceles seen by any one surgeon or by a clinic is relatively small, emphasis should be placed on the correct surgical management of the condition when it does present itself.

Up until the time that Ladd and Gross<sup>2</sup> first published their report of a series of omphaloceles the condition has been designated by a number of terms, which only led to a moderate degree of confusion. Some of these terms are congenital eventration; hernia into the umbilical cord; amniocele or amniotic hernia; funicular hernia of the umbilical cord; exomphalos and, erroneously, umbilical hernia. Ladd and Gross emphasized the use of the term omphalocele as suitable for the condition in an effort to differentiate it from umbilical hernia. This use of a constant term permitted grouping of all the other conditions under a usable and suitable heading. The frequent use of the word "hernia" in so many of these descriptions only led to confusion and a false impression that umbilical hernia and omphalocele were closely allied. At the present, it is well understood that from both an embryologic and an anatomic standpoint the two lesions are entirely different. An umbilical hernia results from an incomplete formation and fusion of normal fascia and muscle layers of the anterior abdominal wall in such a way that a defect is formed at the umbilicus, which after birth may become larger.

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Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

From the University of Louisville School of Medicine and the Surgical Departments of Louisville General Hospital.

1. Margulies, L.: Omphalocele (Amniocele), *Am. J. Obst. & Gynec.* **49**:695-699 (May) 1945.

2. Ladd, W. E., and Gross, R. E.: *Abdominal Surgery of Infancy and Childhood*, Philadelphia, W. B. Saunders Company, 1941.

It is covered by peritoneum, a thin layer of fascia, subcutaneous fat and skin. In direct contrast, an omphalocele consists of a defect in the anterior abdominal wall at the umbilicus with little or no attachment or fusion of the normal fascia of the rectus muscles and extrusion of the peritoneal contents into a sac covered only by peritoneum and amniotic membrane.

At the time of delivery, the membrane is transparent, clear and glistening. Within as short a period as three to four hours this glistening surface becomes dull, gray to green in color and thickened, even though it is kept moist with any type of moist compress. After this time the membrane becomes permeable to bacteria, and fatal peritonitis will necessarily follow unless proper surgical intervention is carried out. Because of this relatively rapid change in the membranous covering of the sac, surgical intervention and repair of one type or another of the omphalocele is necessary within a relatively few hours after delivery. The need for operation within a short time has been brought out by Gross<sup>3</sup> in a recent paper; and here again another plea is made for operation as soon as possible after delivery. It is also desirable to operate on these infants within this short space of time before they have swallowed air or formula, which will, necessarily, distend the intestines which are in the sac and, from a mechanical standpoint, will render repair much more difficult.

The series of events leading up to the formation of an omphalocele begins during the first five to ten weeks of fetal life.<sup>4</sup> At this time, the intestinal tract has grown more rapidly than the future peritoneal cavity, and, since the celomic cavity, or future peritoneal cavity, cannot accommodate the rapidly growing intestinal tract, an embryonic, anatomic—or, more simply, a necessary—umbilical herniation results and the gastrointestinal tract extrudes into the base of the umbilical cord. Under normal developmental conditions, at about the end of the tenth week, the future peritoneal cavity has enlarged enough to accommodate the intestinal tract; it is withdrawn, and the defect in the anterior wall of the abdomen closes. If there is abnormal development of the intestinal tract and lack of growth and provision for space in the future peritoneal cavity or if some other peritoneal growth mechanism stops or is delayed, then an omphalocele may result. From that time until the time of delivery any portion of the intestinal tract, liver or spleen or any mobile intraperitoneal structure may remain in the sac. As a portion of the viscera remains in the sac, there will be no further attempt toward formation of an adequate peritoneal cavity.

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3. Gross, R. E.: A New Method for Surgical Treatment of Large Omphaloceles, *Surgery* 24:277-292 (Aug.) 1948.

4. Arey, L. B.: *Developmental Anatomy: A Textbook and Laboratory Manual of Embryology*, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

Omphaloceles vary greatly in size and in contained viscera. The larger the sac and the greater the amount of contained viscera, the greater the mortality. It has been brought out that omphaloceles 10 cm. and above in diameter may carry a mortality of 85 per cent; however, with newer surgical technics and frequently repeated pleas for earlier surgical intervention, this mortality may well be notably decreased. There are a number of reports in the literature of successful repair of omphaloceles.

Surgical management of an omphalocele as a surgical emergency may be a relatively easy and simple procedure, or it may tax the ingenuity of the surgeon when he is confronted with a tremendous sac containing a large portion of the viscera and a distressingly small peritoneal cavity. In small omphaloceles, in which the diameter of the defect in the anterior abdominal wall is below 4 to 5 cm. and the amount of contained viscera is relatively small, the actual mechanical management of the problem is simple. In omphaloceles of this size it is frequently possible to replace the extruded viscera, excise the covering and close the defect. In cases with these smaller sacs the surgeon will be able to do a layer closure, the resulting closure will be strong and the infant will need no further surgical treatment.

In case of a larger omphalocele with an unruptured membrane, more technical difficulties present themselves, both from a mechanical standpoint and from the standpoint of possibly altering the infant's physiologic processes. When the amount of extruded viscera is greater than the peritoneal cavity, then replacement of this extruded material into the small peritoneal cavity by main force and attempted closure of the defect with the replaced material under a moderate amount of pressure will produce the following alterations in the infant: First, there will be elevation of both sides of the diaphragm, with a decrease in the vital capacity of the youngster; hence a series of pulmonary complications could result, or the infant may even become cyanotic owing to the marked decrease in tidal air and vital capacity. Second, placing the extruded material back into the peritoneal cavity under pressure may produce enough pressure on the inferior vena cava and the mesenteric and portal systems to cause circulatory failure because of this increase in intraperitoneal pressure and compression of these venous systems. Third, replacement of the intestinal tract under pressure may lead to temporary intestinal obstruction.

Ladd and Gross first suggested a two stage operation in order to obviate the possible complications due to overcrowding of the peritoneal cavity at the first operation. Their first suggestion was excision of the sac and covering the extruded material with nothing more than

skin flaps, hoping that in time the peritoneal cavity would enlarge enough and the muscles and fascia would stretch enough so that a satisfactory layer closure could be done. This approach was unsatisfactory because the serosal surface of the intestine was being covered by raw subcutaneous fat, which naturally led to multiple adhesions between the loops of intestine and the under surface of the skin flaps; consequently, at the time of secondary operation the dissection of the loops of intestine from the under surface of the skin flaps turned the second procedure into an operation of greater magnitude. Recently, Gross has suggested management of this situation by a method which seems to be much more logical. In his recent cases he has left the membranous sac undisturbed and has merely dissected up lateral skin flaps and brought them over the intact membrane after excision of the cord and then closed the skin flaps over the membranous sac. Theoretically, this would prevent adhesions between the loops of intestine and the skin flaps and make the secondary procedure much simpler, after the muscles and fascia had stretched enough to accommodate the extruded viscera.

In cases in which the membranous covering has ruptured either before or at the time of delivery, the surgeon is confronted with a different problem. There is no membranous covering to protect the intestines from adhesions; hence the surgeon either will have to replace all the eviscerated material and do a layer closure, or if this is impossible will be forced to resort to Ladd and Gross's original suggestion and merely cover the intestines with the raw flaps. In the latter procedure, he will again be faced with multiple adhesions between the skin flaps and the intestinal wall at the time of secondary operation. At the present time no suitable covering has been developed for use as a barrier between the loops of intestines and the raw surfaces of the flaps. Apparently, the use of any of the present oxidized cellulose or gelatin preparations would not be the answer, since it has been demonstrated that as the absorbable material disappears it is replaced with fibroblastic material with the result that after absorption of the material adhesions will still form between the intestine and raw surfaces of the skin flaps.

Recently I have seen a number of omphaloceles that have required several different technics in surgical repair. In the following case reports I am reporting only those cases which demonstrate different technics.

#### REPORT OF CASES

It has been generally agreed previously that intrauterine rupture of an omphalocele or rupture at the time of delivery carried practically a 100 per cent mortality. I feel that this has been true in the past because too long an interval has been allowed to elapse before surgical

repair was attempted; also, it has been probably true that in cases in which rupture had occurred the intestinal tract and other extruded viscera have been replaced under tremendous pressure and death of the infant was secondary to one or a combination of the three factors mentioned.

Following is a report of successful repair of an intrauterine rupture of an omphalocele.

CASE 1.—Baby boy H., was delivered at 4:15 a. m. on Sept. 12, 1948. The mother, a primipara and primigravida, was at term and had been in labor approximately thirty hours at the time of delivery. Examination within fifteen minutes

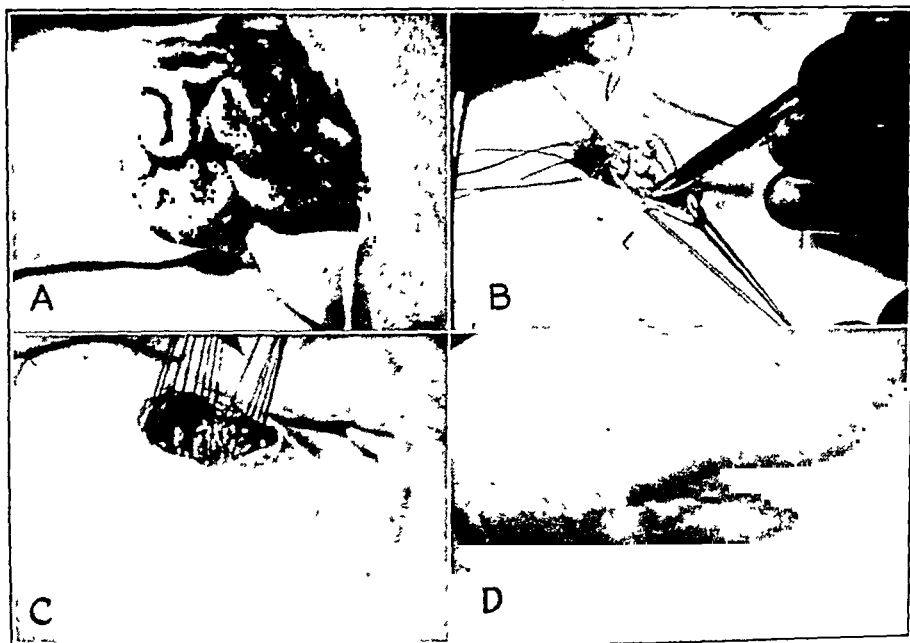


Fig. 1 (case 1).—*A*, amount of extruded viscera. *B*, closure of the peritoneum after replacement of the intestinal tract. *C*, appearance after the edges of the sheath of the anterior rectus muscle have been freshened up and 0000 silk sutures have been placed. *D*, strong anterior abdominal wall at the end of five months. (Reproductions from kodachrome® movie film.)

after delivery revealed that the infant was normal except for the presence of almost the entire intestinal tract herniated through a defect measuring approximately 6.5 cm. in diameter (fig. 1 *A*). Apparently, the omphalocele had ruptured early in labor because the individual loops of small bowel were covered with fairly well organized fibrin. Remnants of the membranous covering of the omphalocele were still attached to the margins of the defect, and the umbilical cord was attached to the left side of the opening. Surgical repair was begun within an hour after delivery. The intestines were gently but thoroughly cleaned with warm isotonic sodium chloride solution and further cleansed by application of aqueous merthiolate.<sup>6</sup> The intestinal tract was replaced with moderate difficulty, but after replacement the peritoneal cavity seemed to be adequate in size and it was felt that undue pressure on the diaphragm, vena cava and portal systems would not be produced.

The edges of the defect were trimmed away, and the peritoneum was closed with continuous suture of 000000 surgical gut (fig. 1 *B*). Edges of the anterior rectus sheaths were then dissected up and closed with 0000 silk (fig. 1 *C*) and the skin defect closed with interrupted silk sutures.

For the first forty-eight hours no milk or formula was given the infant, in order to decrease the amount of distention of the intestinal tract. During this period he was given adequate amounts of fluids subcutaneously and intravenously. After this initial bit of starvation, the infant was started on very small feedings, supplemented with fluids by the subcutaneous and intravenous routes. This regimen was followed for four days, after which time the infant was placed on regular feedings. His postoperative course was entirely satisfactory, and he was discharged from the hospital on the fourteenth postoperative day. His development since that time has been entirely normal, and when last seen, five months after repair, he presented a strong anterior abdominal wall (fig. 1 *D*).

This next case report concerns an infant born with a tremendous omphalocele and a peritoneal cavity much too small to accommodate the extruded material. Unfortunately, I was not called until about six

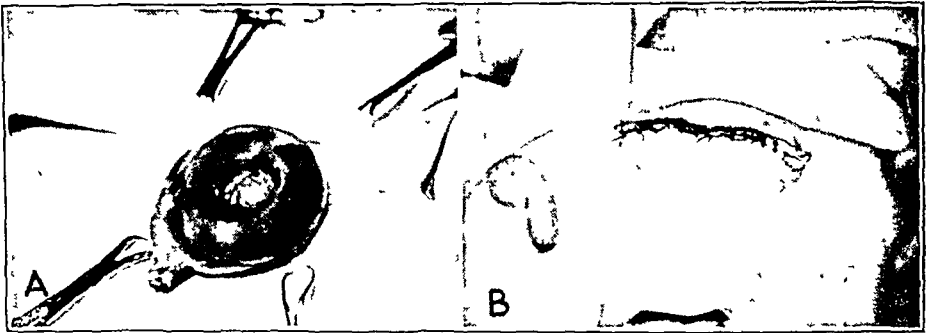


Fig. 2 (case 2)—*A*, preoperative photograph showing the thickened, discolored membranous covering. *B*, appearance of the patient at the end of the operation, done according to the technic recommended by Gross.

hours post partum. Even though the sac had been kept moist with saline compresses during that time, it was very thick, gray-green and obviously permeable to bacteria.

**CASE 2**—Baby boy M. was a full term infant. Delivery was difficult because of the omphalocele present. Examination six hours after delivery revealed a 7 pound 6 ounce (3,345 Gm.) child that was normal except for the omphalocele (fig. 2 *A*). The membranous covering of the omphalocele was thickened and discolored. It measured approximately 13 cm. at its base and obviously contained a large portion of the gastrointestinal tract as well as a large portion of the right and left lobes of the liver. An operation was carried out approximately seven hours after delivery. The membranous covering of the omphalocele was thoroughly cleansed with very dilute soap and water and then cleansed with aqueous merthiolate® solution. It was obvious that the peritoneal cavity was too small to accommodate all the viscera contained in the sac; therefore, following the technic advocated by Gross, the membranous covering was not disturbed. Dissection was begun at the junction of the skin and membranous covering and wide undermining of the skin produced skin flaps large enough to allow bringing the skin edges



together over the mass and approximating them without tension (fig. 2 B). The immediate postoperative condition of the infant was satisfactory; however, within twenty-four hours after delivery, the infant began to run a septic course and died within fifty hours following operation. The contained viscera were not under undue pressure, since the infant was able to take his feedings regularly and was having normal meconial stools up until twelve hours prior to death.

This infant obviously died from acute fulminating peritonitis, and his case demonstrates how permeable the membranous covering of the omphalocele will become to bacteria within a relatively few hours after delivery.

One of the biggest problems that will confront the surgeon will be the newborn with a ruptured omphalocele in which the defect is large and the amount of extruded viscera is too great to replace without running the danger of one or more of the three complications previously mentioned. In such a case the only type of repair that can be done is dissection of skin flaps large enough to cover the intestine and other extruded viscera, with no attempt directed toward repair of the defect itself. This, necessarily, will lead to troublesome adhesions and a more difficult secondary repair.

CASE 3.—Baby boy S. was born prematurely at approximately seven and one-half months with a tremendous defect measuring approximately 7 cm. in diameter. The membranous covering of the omphalocele was ruptured, and it is more than likely that it had ruptured during labor and before delivery, since the individual loops of intestine were covered with fairly firm fibrin. It was obvious at the time of operation that the peritoneal cavity was too small to accommodate these viscera. Since the membranous covering had been destroyed, the only method of repair left was to attempt a skin covering. Accordingly, lateral skin flaps were dissected up and the viscera covered with these raw skin flaps, with the skin closure under no tension. This infant's immediate postoperative condition was fairly good, and for approximately four days he seemed to be on the road to recovery; however, from this time until the time death, six days later, his course was gradually downhill. Apparently, prematurity was the biggest factor in this infant's death, since during the entire postoperative period he had been able to take most of his feedings and was having fairly normal small stools.

#### SUMMARY

1. The embryologic and anatomic features involved in an omphalocele are discussed.
2. A plea is made for early surgical repair.
3. The types of repair which may be necessary are described and illustrated by case reports.
4. Successful repair of an intrauterine rupture of an omphalocele is described.

## NEW SURGICAL PROCEDURES IN CERTAIN CASES OF CONGENITAL PULMONARY STENOSIS

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AND

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**T**HE TECHNIC of subclavian-pulmonary or aortic-pulmonary anastomosis for the classic case of congenital pulmonary stenosis has been fairly well standardized. Unpredictable findings at operation necessitate use of improved variations in surgical procedures. The following 2 cases illustrate emergency deviations in surgical technic necessitated by anomalies of the pulmonary artery.

CASE 1.—T. K., a girl aged 7 years, weighing 43 pounds (19.5 Kg.), was admitted to the Children's Memorial Hospital, Oct. 12, 1948. She had been mildly cyanotic since birth, became dyspneic on slight exertion and after walking about one block would squat in characteristic fashion.

Physical examination revealed a frail child with cyanosis visible only in the lips, fingers and toes. Suffusion of the conjunctiva was moderate; clubbing of the fingers and toes was minimal. A loud, harsh systolic murmur was heard at the left third interspace along the edge of the sternum. An accompanying thrill was palpable.

Fluoroscopic and roentgenologic examination of the chest revealed a typical boot-shaped heart, avascular pulmonary fields, a rather indefinite pulmonary window and a right-sided aortic arch. The electrocardiogram showed deviation of the axis to the right. The red blood cell count was 6,020,000; the hemoglobin content was 16.4 Gm.

A diagnosis of tetralogy of Fallot with deviation of the aorta to the right was made by Dr. Stanley Gibson. The patient was classed as a good operative risk. Because of the right arch it was decided to perform a subclavian-pulmonary anastomosis on the left side.

*Operation* (by W. J. P., Oct. 14, 1948.)—Under cyclopropane-oxygen anesthesia administered by Dr. William O. McQuiston, the chest was opened through a posterolateral incision in the left fourth interspace. Sufficient exposure was obtained by separating the ribs with a rib spreader.

The left pulmonary artery was dissected from its bed; it was huge, measuring 1.5 cm. in diameter. A very brisk systolic thrill was palpable at the base of the heart at the point of emergence of the main pulmonary artery.

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From the Children's Memorial Hospital and Grant Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

The subclavian artery was isolated and the encircling recurrent laryngeal nerve identified and freed from the adventitia. The subclavian artery was ligated at its point of branching and a ductus clamp<sup>1</sup> applied about 1.5 cm. proximal to the ligature. The artery was then cut just proximal to the point of ligation and drawn out of the loop of the recurrent laryngeal nerve. It measured 6 mm. in diameter.

Constricting ligatures were put around the branches of the left pulmonary artery in preparation for the anastomosis. Very promptly the child showed signs of severe anoxia. The heart slowed and became irregular and the blood pressure dropped alarmingly. The ligatures were promptly released. The aortic clamp was then applied to the pulmonary artery, and a small segment of the vessel

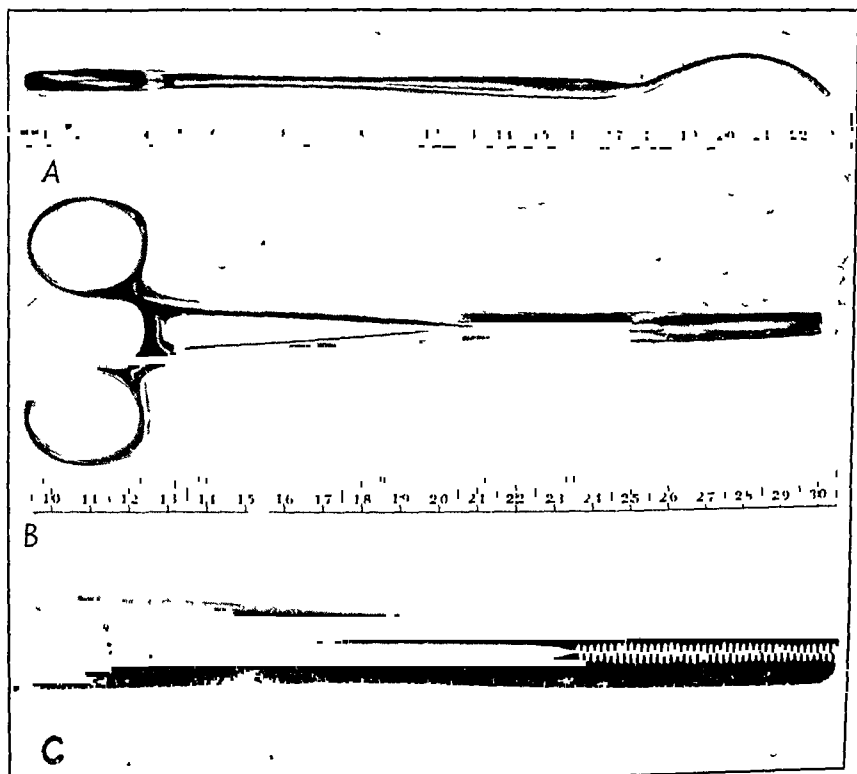


Fig 1—*A* and *B*, two views of the curved clamp showing the multiple fine teeth in the apposing jaws. These teeth embed themselves in the adventitia and will occlude but will not injure the vessel. *C*, an enlargement of the ductus clamp to illustrate the arrangement of teeth. There are 40 fine teeth to the inch (2.54 cm).

was clamped off. Fortunately, before a cut was made in the pulmonary artery, traction was made on the clamp to bring the vessel toward the end of the subclavian artery. As soon as slight traction was made, all signs of severe anoxia promptly returned. A second attempt with similar results made it obvious that very little encroachment on the blood flow in the left pulmonary artery was permissible.

1 Potts, W. J.: A New Clamp for Surgical Division of the Patent Ductus Arteriosus, *Northwestern Univ. Med. School Quart. Bull.* 22:321 (Nov.) 1948.

A curved instrument (fig. 1) embodying the same principle as the ductus clamp previously described<sup>1</sup> had been made for a different purpose. The jaws of the clamp are fashioned with many fine teeth which grasp the vessel and occlude it, will not slip and will not injure the vessel. This curved clamp was applied to the left pulmonary artery longitudinally, pinching off a small lateral segment of the vessel (fig. 2). A 6 mm. incision was made in this occluded portion of the pulmonary artery, and an end to side anastomosis was made between it and the proximal end of the subclavian artery. Because the isolated segment of pulmonary artery was small, it was impossible to make the anastomosis intima to intima. The end of the subclavian artery was sutured to the pulmonary artery

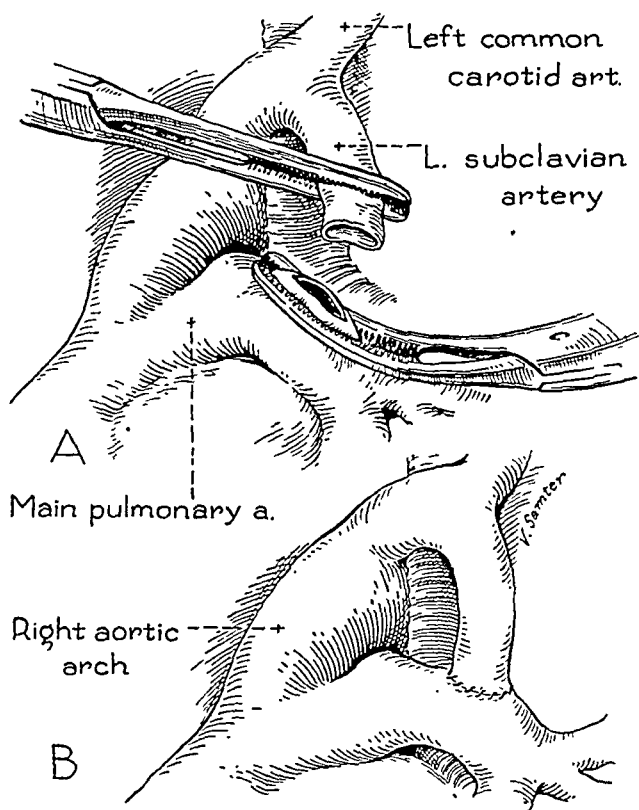


Fig. 2.—*A*, the curved clamp tangentially applied to the pulmonary artery allowing a good portion of the blood to continue to flow through the vessel while the anastomosis is being made. *B*, anastomosis between the subclavian and the pulmonary artery completed with a continuous over and over stitch.

with a single row of continuous over and over stitches of 00000 Deknatel silk. On release of the clamps, there was no bleeding and a brisk continuous thrill was palpable over the anastomotic site. Except for those episodes of anoxia which occurred when the pulmonary blood flow was interfered with, the child withstood the operation well.

The chest was drained with a de Pezzer catheter introduced through the sixth interspace and later connected with a water seal bottle. The lung was reexpanded and the wound closed.

The postoperative course was uneventful. The child was routinely kept in oxygen for twenty-four hours and given 100,000 units of penicillin twice daily for one week. A continuous murmur characteristic of such blood vessel anastomoses could be heard clearly over the left side of the chest anteriorly and posteriorly. All visible cyanosis was relieved. The patient was discharged on the fourteenth day after operation in excellent condition.

On Feb. 4, 1949 the mother reported by telegraph that "Treva walks five blocks to school and back each day. Plays with the other children without restriction. Her color is just like everybody else's. Her appetite was poor but has improved now, and she is doing fine generally."

CASE 2.—L. G. Jr., aged 19 years, entered Grant Hospital Oct. 3, 1948, complaining of slowly increasing cyanosis since infancy and greatly reduced tolerance for exercise. His physical and mental development had been normal.

Physical examination revealed a young man deeply cyanotic with marked clubbing of the fingers and toes and suffusion of the eyes. His weight was 155 pounds (70.3 Kg). His blood pressure was 110 systolic and 85 diastolic. A loud systolic murmur was heard at the second interspace to the left of the sternum. Fluoroscopic and roentgenologic examination of the chest revealed a somewhat enlarged heart which was not typically boot shaped, avascular pulmonary fields, pulmonary window and a right aortic arch confirmed by barium swallow. The electrocardiogram showed deviation of the axis to the right. The red blood cell count was 6,060,000 and the hemoglobin was 18 Gm. A diagnosis of tetralogy of Fallot with a right aortic arch was made by Dr. Frank Dammann.

*Operation* (by S. S., Oct. 5, 1948).—With the patient under cyclopropane-ether-curare anesthesia, a posterolateral curved subscapular incision was made on the right side. The chest was entered through the base of the fourth rib resected subperiosteally. Cyanosis increased perceptibly when the chest was opened. A large pulmonary artery was identified and dissected from its bed. Complete occlusion of the right pulmonary artery caused immediate cardiac embarrassment. Three times the pulmonary artery was occluded, and each time the heart practically stopped. It was obvious that occlusion of the entire right pulmonary artery for the time necessary to perform an aortic-pulmonary anastomosis or a subclavian-pulmonary anastomosis would not be tolerated.

Dr. McQuiston suggested that the proximal end of one of the branches of the pulmonary artery to the upper lobe might be anastomosed to the side of the aorta. Such a procedure would allow blood to flow through most of the pulmonary artery to the lower and middle lobes while the anastomosis was being made. The large divisions of the pulmonary artery in the hilus of the lung were dissected out, and a branch 5 mm. in diameter, to a segment of the upper lobe of the lung, was chosen. The vessel was occluded proximally with a ductus clamp,<sup>1</sup> ligated distally and cut between. The aortic clamp was applied to the aorta, and in the occluded segment a 5 mm. incision was made (fig. 3). The proximal end of the branch of the pulmonary artery was then anastomosed to the side of the aorta. A silk suture was placed at each end and the anastomosis completed with a single row of continuous 00000 Deknatel braided silk on a curved no. 9 needle. Technically, it was rather difficult to suture the thin-walled pulmonary artery to the thick-walled aorta, but on release of the clamps there was little bleeding and a brisk thrill was palpable over the anastomotic site as blood flowed from the aorta into the pulmonary system. The patient's condition improved immediately.

The lungs were reexpanded. A de Pezzer catheter drain was placed in the sixth interspace and the chest closed in layers with a running suture of surgical gut. The drain was later connected with a water seal bottle.

The postoperative course was uneventful. The drain was removed on the third day. On the patient's discharge from the hospital twelve days after operation, cyanosis was relieved. The red blood cell count had fallen to 5,120,000 and the hemoglobin to 14.6 Gm.

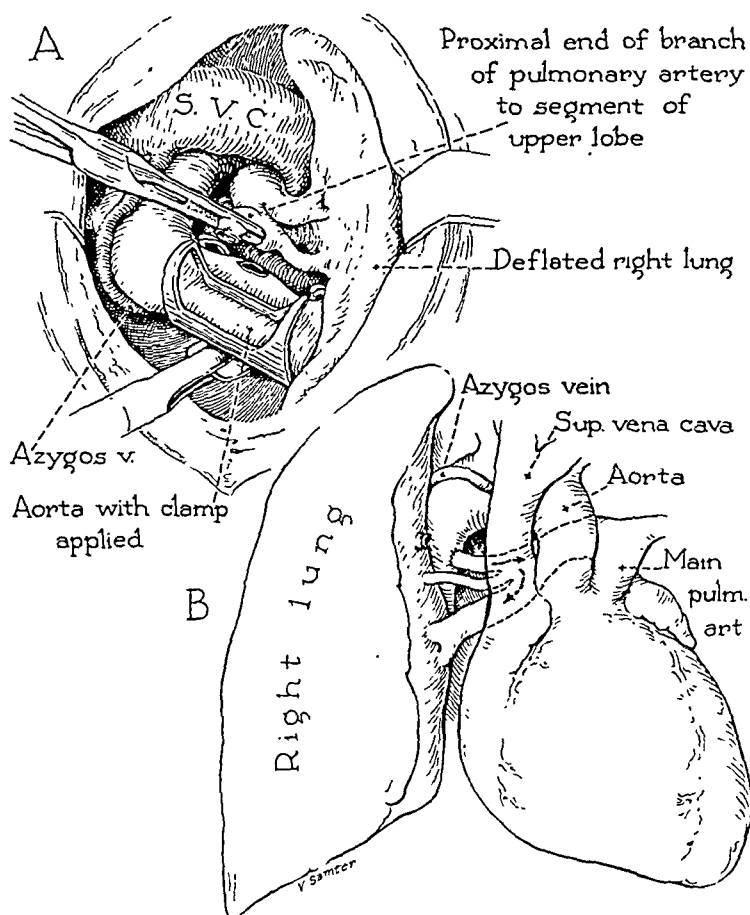


Fig. 3.—*A*, the proximal end of a branch of the pulmonary artery is being held with a ductus clamp. The distal end of this branch has been ligated. A segment of the aorta has been isolated, and a 5 mm. long incision has been made in it. *B*, the anastomosis between the proximal end of a pulmonary artery and the aorta has been completed with an over and over continuous silk suture.

The patient when last seen, Jan. 29, 1949, was in excellent health. No cyanosis was visible, and the tolerance for exercise was tremendously improved. The loud, continuous murmur heard immediately after operation over the right side of the chest has persisted, indicating that the anastomotic channel has remained patent. Little enlargement of the heart has occurred thus far. Clinical and roentgen examinations indicate that no difficulties have arisen from ligating a branch of the pulmonary artery to a segment of the upper lobe.

## COMMENT

The fundamental problem in the 2 cases was the same—occlusion of a pulmonary artery for the length of time necessary to perform an anastomosis could not be tolerated. In each case, some blood had to flow continuously through the pulmonary artery to which the systemic vessel was being anastomosed. It must be assumed that in case 1 the left pulmonary and in case 2 the right pulmonary artery were too small to carry enough blood to the lungs to sustain life.

By means of a narrow curved clamp with many fine teeth in the apposing jaws, a crescent-shaped segment of a pulmonary artery may be isolated for anastomosis to a systemic vessel.

It appears from case 2 that the proximal end of a branch of the pulmonary artery may be satisfactorily used for diversion of blood from the systemic to the pulmonic circulation.

## DISCUSSION OF PRECEDING PAPERS

DR. LEON S. MCGOOGAN, Omaha: I should like to comment on the paper by Dr. McLachlin, of Canada, on "Duodenal Obstruction in the Newborn." It has been my unfortunate experience to find that most of the children that I have personally delivered have had multiple lesions of the small bowel and have not been amenable to surgical treatment, and I should like to emphasize again that when one congenital anomaly is found in a newborn infant that a very careful survey be made of the whole child to find other congenital anomalies which may, of course, bar surgical intervention or even any attempt at operation.

As an obstetrician I should like to ask Dr. Maguire what dressing should be placed on an omphalocele sac until the surgeon can get there. Should it be a simple wet saline dressing? Should there be added to the dressing any material such as penicillin until the surgeon can repair the defect?

Is an omphalocele an absolute emergency? Should the surgeon be called within a period of fifteen or thirty minutes after delivery? In case there is a ruptured sac or such a thin sac that there can be no imposition of peritoneum with the closure of the abdomen, is it possible to use transplant of fetal membrane from the placenta? Could the fetal membranes be separated from the placenta and preserved in some sort of solution and used as a graft to help fill in the defect where the peritoneum cannot be used?

DR. CLIFFORD D. BENSON, Detroit: I have observed, as Dr. McLachlin has stated, that obstructions of the duodenum are certainly commoner than was formerly believed. They occur about once in 20,000 cases, and during the past eighteen months I have had 4 cases in addition to those which I reported before this Association two years ago.

I should like to say a few words concerning Dr. Maguire's paper on omphalocele. As he has mentioned, there is a tendency to combine hernia into the umbilical cord and omphaloceles into one group. That may be all right, but I believe that

there is a great difference between hernia into the umbilical cord and omphalocele embryologically. Hernia into the umbilical cord occurs in the eighth to tenth week of embryonic life, whereas omphalocele occurs in the third week. In hernia of the umbilical cord, the problem is one of simply excising the sac and closing the defect, which is a small defect, usually less than 4 cm. in length, where as in the true omphalocele there is a defect of the anterior abdominal wall. In the latter case there is a large defect to be closed, and it presents an entirely different problem. There is a possibility of infection, and also if the sac is not open one will overlook other anomalies which occur in about a third of these patients. In other words, there may be an atresia or stenosis of the intestine. Some of these large defects, 9 or 10 cm. in diameter, cannot be closed in layers; hence we have elected to close them simply by skin closure.

When should one do the second stage closures? That should be determined when one can reduce the contents of the herniation into the abdomen without any discomfort or embarrassment as far as respiratory system is concerned. That must be postponed from six months to twelve months or longer in the large defects.

DR. EDWIN M. MILLER, Chicago: This interesting symposium on children's surgery well exemplifies the rapidly increasing and widespread interest that has been developing in this field since the first successful report of operation for congenital duodenal atresia, by Ernst of Copenhagen in 1916.

There are two points in regard to the paper presented by Dr. Maguire which are worthy of a little more emphasis. First, with due respect to the opinion of D. Penberthy and Dr. Benson, I believe very strongly that it is a good idea wherever possible to maintain intact this delicate cellophane-like transparent covering for the viscera in the infant born with the large omphalocele. Too often this has already been ruptured when we first see these little patients, or too often, therefore, peritonitis is already present. The need for immediate operation is quite apparent, and the objective is to secure a covering of skin, as Dr. Maguire has so well shown in his colored movie. These wounds, because of tension, do not always heal by primary union, and some of the stitches gradually give way leaving areas of granulation tissue which become covered slowly by a rough, thick, epithelial surface.

Second, there is no hurry, as I see it, about performing the second operation. In fact, it is wise to allow several months, or better still, several years to pass by, and during this waiting period good use is made of a wide elastic supporting band. One of my little patients, upon whom I operated in 1933, now is a full grown young woman and well illustrates the good result which can be obtained by observing the points which we have here endeavored to stress.

DR. R. K. GILCHRIST, Chicago: I emphasize some points of our case of tracheoesophageal fistula because the diagnosis is so easily missed. This man had several drinks, but he was not really drunk when he was brought to the hospital. He was not sick. He was not knocked out. He had coughed up a little blood. I did not see him until two days later. No one thought much about it until the second morning, when Dr. Albi said, "When he drinks he strangles." They had just given him a swallow of iodized oil which filled the lower bronchi. He had no emphysema. The fistula occurred at exactly the same spot where a similar one occurred in a man in the Navy who had a heavy box strike him a glancing blow across the upper part of the chest. That man manifested emphysema, and he had to have a tracheotomy before his fistula was repaired. This tear



occurs where the trachea and the esophagus are in their most intimate contact. I suppose that there is some sort of hyperextension mechanism pulling downward that snaps the trachea and esophagus like a rubber band and tears them. Obviously, chemotherapy helped prevent mediastinitis, but if the diagnosis had been made in the first few hours the treatment would have been different. I am also sure that the feeding by the tube passed beyond this fistula is not a particularly safe one and one is better off to do a gastrostomy and feed the patient immediately.

There is no particular trick to doing the operation as far as separation of the tract goes, since there is good firm scar tissue; there is also no likelihood of stirring up a still dormant infection. The mediastinal pleura should be left open after the tract has been separated so that mediastinitis does not develop if there is a leak.

We think that in this patient—who was not a good patient and who was a prisoner of the police under arrest at the time and who rejected everything that was done—the interposition of the flap of pleura probably prevented the reestablishment of the fistula when he was eating food that was brought to him on the side by his family. He is perfectly well now.

DR. JOHN K. ORMOND, Detroit: As one of the very few urologists who are members of this Association, I should like to congratulate Drs. Lich, Maurer and Burdon on their presentation. I was particularly interested in their application to children. It is very promising. As a background, I might state that I have tried the method they spoke of only 3 times. My colleagues and I still use the one stage suprapubic prostatectomy in about half our cases. In a little less than half we have used the transurethral operation route, saving the perineal route for the radical procedures for carcinoma.

One thing that has given us pause in adopting the retropubic method is the fear of osteitis pubis. I notice in their report that the authors spoke of having seen a certain number of cases of osteitis pubis. I should like to ask them to say how quickly it occurred and how long before the patients recovered.

DR. ROBERT M. WANSBROUGH, Toronto, Canada: I am always stimulated by my old colleague, Dr. McLachlin, because he delves into things that many persons neglect. The duodenal atresias are not rare at all; they are just not diagnosed. This is truer in a large number of lesions in children than it is in adults. There are two or three things that Dr. McLachlin spoke of that I feel are very important. In new babies, the vitality is low and they are suffering from malnutrition. I therefore feel it is most important that the viscera are handled very gently, and, as many of these patients have some degree of failure of rotation, I do not believe it is wise to attempt to return the viscera to a normal anatomic position.

DR. HENRY K. RANSOM, Ann Arbor, Mich.: I should like to comment on Dr. Leahy's paper and report a case that I observed last year, a case of congenital pulmonary tension cyst in a little child  $3\frac{1}{2}$  months old. The child was brought in cyanosed, presenting a typical picture. A roentgenogram showed the mediastinum pushed far over to the opposite side and a needle was inserted into the cyst for the immediate relief. The child at the time it came in had a little fever (temperature up to 100.1 F.). There were rales on his good side and marked atelectasis in both upper and lower lobes of both lungs so one could hardly see the lobes and would not be sure they were present on the first roentgenogram. With repeated films one could tell that the upper and lower lobes were present and that the cyst probably arose from the middle lobe. We kept

the child under aspiration until his temperature came down to normal, approximately five or six days, and took out the cyst. The cyst was unbelievably simple to remove. The minute I made an anterior incision across the front of the chest—and the needle was out of the cyst at that time—the cyst ballooned right out, and it was practically unnecessary to use a retractor. The child's face was a little blue on the second day. The needle stopped draining, and I suggested that a tube be put in. I took the child to the dressing room, made a little niche, put in a trocar and slipped the tube in 3 or 4 cm. and the air came back into the bottle. Next morning the attendants said that air had stopped coming through the tube. The child was just starting to get blue again. We checked immediately with the roentgenogram, and the tube was lying between two layers of pleura outside the cyst, and the air had been leaking through and in that had become blocked off.

DR. ANTHONY R. CURRERI, Madison, Wis.: From the several papers presented this morning, it must be obvious that, at least in so far as operation in young infants is concerned, procrastination is not indicated. I should like to say a little more about Dr. Leahy's paper. Undoubtedly, with the combined efforts of surgeons, pediatricians and anesthetists many infants can have the advantage of exploration with minimal injury and with an opportunity to obtain excellent results. Thoracic lesions mimic one another. For example, emphysema may mimic tension pneumothorax. A mediastinal gastric cyst has masqueraded as pneumonia and whooping cough in one of our cases, and other mediastinal cysts have been considered thoracic tumors. Congenital cysts are often treated by physicians by procrastination and conservative therapy until secondary infection occurs. At this time, everyone is excited and immediate operation is requested. Here the problem is one of resection when the cysts are free from infection. At that time operation is simple, and the child's immediate postoperative course excellent. Surgical procedures during a period of acute infection are associated with toxemia, acute inflammatory reaction and nodes about the hilar structures. Thus, dissection of the bronchi and vessels is extremely difficult and the immediate postoperative course is much more violent.

DR. ROBERT LICH, Louisville, Ky.: In regard to Dr. Ormond's questions, I should like to say that in our own work the number of transurethral resections is approximately 40 per cent. When we started our series of retropubic prostatectomies eighteen months ago, we did the first 100 prostatectomies by this method more or less to determine the limitations of this operation.

In so far as osteitis pubis is concerned, this condition occurred in 2 patients. The first patient was hugely obese and severely diabetic and was incapacitated almost 100 per cent, I should say, for a matter of about five weeks, and thereafter he was only partially incapacitated. The other was a man who had very little actual incapacitation. He was able to carry on his usual activities, although he complained of considerable pain in the pubic region. I cannot go into the cause and the whole problem of osteitis pubis, but I should like to mention that one of the severest instances of osteitis pubis that I have ever seen followed a perineal prostatectomy in which the patient was hospitalized intermittently for almost six months. I noticed recently that Drs. Rosenberg and Vest reported 2 instances of osteitis pubis following transurethral resection.

In conclusion, one can only say that to date in the American literature osteitis pubis constitutes the greatest hazard to retropubic prostatectomy. Our experience, however, has not been sufficiently alarming to discard the operation.

DR. WINFIELD L. BUTSCH, Buffalo: It seems to me that aspiration of pulmonary cysts carries with it considerable danger: first, that the aspiration may be followed by an immediate collapse of the lung and pneumothorax, thus precipitating a respiratory crisis, and, secondly, that the procedure may be followed by infection with toxemia. The delay connected with aspiration may also be accompanied with infection in other portions of the lung, due to the continued pressure of the cyst. Therefore, Dr. Butsch and I agree with the discussers that aspiration should be used either not at all or only for a temporary period to allow adjustment of the infant's physiologic state. We have found 4 instances in the literature of the removal of lungs or lobes in infants under 1 month of age, to add to the 3 that we reported today. Dr. Gross performed a pneumonectomy on the infant at the age of 3 weeks; Dr. Bailey, lobectomy of the right upper and middle lobes at the age of 1 month; Dr. Chisholm, lobectomy at the age of 5 days, and Dr. Burnett, lobectomy at the age of 15 days. All these operations were successful.

DR. A. D. McLACHLIN, London, Ontario: Dr. Benson has asked about the comparative value of duodenojejunostomy and gastrojejunostomy. The second patient had had a duodenojejunostomy first and then a gastrojejunostomy because the duodenojejunostomy had not functioned within what we thought was an adequate amount of time. At the end of a year, however, roentgenograms showed that only the anastomosis between the duodenum and jejunum was functioning. If the fine catheter had been passed through the duodenojejunostomy, it is unlikely that the second operation would have been necessary.

Dr. Miller spoke of the possibility of other anomalies in these patients. I believe we were rather lucky here in having 4 cases with what seems a single congenital defect. Three of the patients are now more than a year old and are making apparently normal progress.

I agree with Dr. Wansbrough regarding the necessity for gentleness in children's surgery. The last of these patients had almost succumbed to exploration in the depths of the abdomen. Four days later this same baby, still having had no food by mouth, underwent a duodenojejunostomy in which there was no other handling with minimal disturbance. It seems that children are superior to adults in surviving operative procedures in everything except their ability to stand rough handling. If the operative procedure can be completed with a minimal amount of trauma, their chance of survival seems greater than in the adult.

DR. C. H. MAGUIRE, Louisville, Ky.: In regard to Dr. McGoogan's question as to what dressing should be placed on the omphalocele, I do not consider that of too much importance. In the second case, in which the membranous covering was quite thick and dirty gray, that youngster had been kept with a saline compress from the time of delivery until it was decided what to do. One wonders whether the use of any antibiotic as a compress might not irritate the membranous covering which, after all, is nothing more than peritoneum.

To the question as to whether or not an omphalocele is an absolute emergency I think the answer is yes. The longer one delays, the less the chance of recovery. Several surgeons have tried letting the big omphaloceles go for a period of weeks, and practically all the cases have ended fatally.

The skin makes an effort to climb over this membranous covering, but in practically all cases of that sort ulceration of the membranous covering occurred and the patients died of the ensuing peritonitis. I was interested in the possibility of the use of the fetal membrane. I certainly think that is one thing that might be considered. As far as I know, nobody has tried it.

I agree with Dr. Benson that a simple herniation into the umbilical cord is not an omphalocele and does not require an extensive surgery.

I agree with Dr. Miller, and take issue with Dr. Benson, in that I do not believe that we should sacrifice the membranous covering, even with the possibility of carrying in a little infection. The use of the membranous covering certainly makes the secondary operation much simpler.

Interestingly, in the infant who died of fulminating peritonitis the space between an apparently dirty membranous covering of the omphalocele and the subcutaneous fat was entirely clean. The infection had already gone through the membranous covering prior to operation. It was not the introduction of the membranous covering into the wound that brought peritonitis.

## A METHOD FOR CONTROL OF BLEEDING FROM ESOPHAGEAL VARICES

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AND

CHARLES G. JOHNSTON, M.D.

DETROIT

ONE OF the most dramatic and hazardous types of bleeding from the gastrointestinal tract is that from esophageal varices. Esophageal varices commonly occur in association with cirrhosis of the liver. In such instances the dilated esophageal vessel is a reflection of increased tension in the portal system. Several methods have been devised for controlling hemorrhage from varices, most of them being a direct attack on the varix itself. In 1939 Crafoord and Frenckner<sup>1</sup> described the nonsurgical treatment of varicose veins by injection of a sclerosing solution under direct vision. Phemister<sup>2</sup> in 1947 reported 1 case with treatment by total gastrectomy and 1 with treatment by esophagogastric resection for bleeding esophageal varices in Banti's syndrome. None of these methods attempt to control the cause of the varix but, rather, attempt to treat the varix itself by removal of the dilated veins or by an attempt to cause clotting within the veins. More recently the work of Blakemore<sup>3</sup> has suggested a method for lowering the portal pressure by means of portacaval or splenorenal vein anastomoses. It has been our experience that bleeding from esophageal varices has provided us with the most clearcut indication for anastomoses between the portal and the caval systems. For such procedure it is best that the patient be in as good condition as is possible. Our interest was turned to a

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Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 18, 1949.

From the Department of Surgery, Wayne University College of Medicine, and the Veterans Administration Hospital, Dearborn, Mich.

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1. Crafoord, C., and Frenckner, P.: Non-Surgical Treatment of Varicose Veins of the Esophagus, *Acta Oto-Laryng.* **27**:422, 1939.

2. Phemister, D. B., and Humphreys, E. M.: Gastro-Esophageal Resection and Total Gastrectomy in the Treatment of Bleeding Varicose Veins in Banti's Syndrome, *Tr. Am. S. A.* **65**:17 (Oct.) 1947.

3. Blakemore, A. H.: Portacaval Anastomosis, *Surgery* **24**:480 (Sept.) 1948.

controllable method of hemostasis in order that patients might be preserved for study and be prepared for portal decompression.

This problem has received attention from several investigators. Westphal,<sup>4</sup> in 1930, used tamponade for bleeding esophageal varices by means of the Gottstein sound. He reported 2 cases in which control

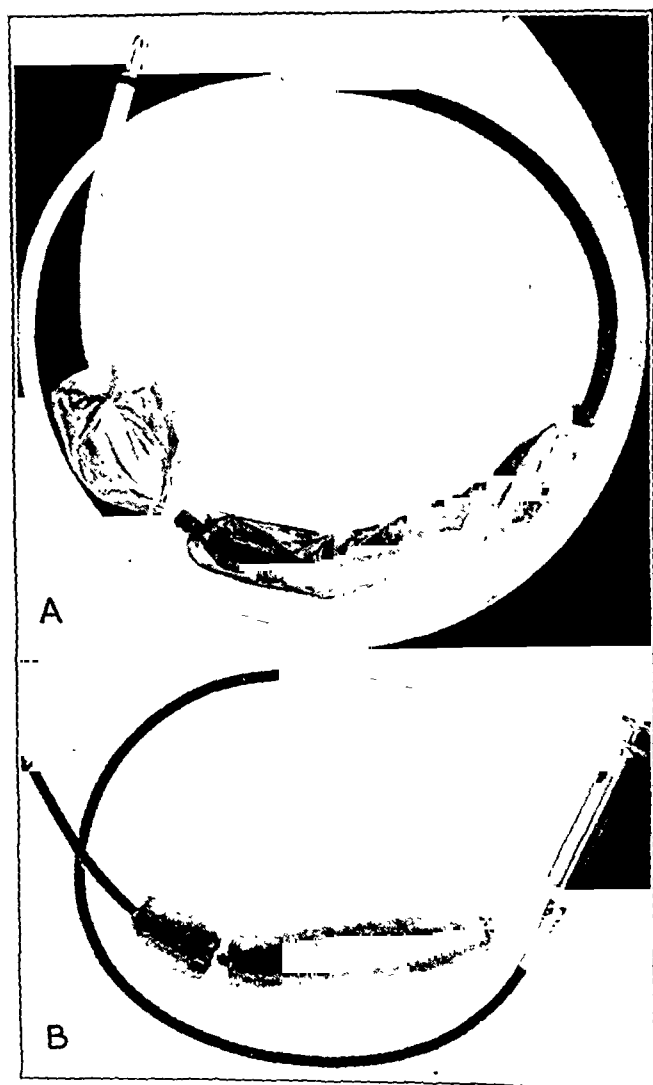


Fig. 1.—Double balloon tube, A, and, B, inflated.

of the bleeding was secured. As far as we can determine, this method received little attention, being mentioned by Kaplan<sup>5</sup> in 1941. In 1947,

4. Westphal, K.: Compression Treatment in Hemorrhage from Esophageal Varix, *Deutsche med. Wchnschr.* 56:1135 (July 4) 1930.

5. Kaplan, B.: Esophageal Varices, *M. Rec.* 154:176 (Sept. 3) 1941.

Rowntree<sup>6</sup> and his associates described an inflatable balloon used to control bleeding from esophageal varices in two cases. Tocantins,<sup>7</sup> in 1948, mentions the use of the balloon tampon for control of esophageal hemorrhage, and Bixby,<sup>8</sup> in the same year, described the use of the Miller-Abbott tube for control of hemorrhage from the same area.

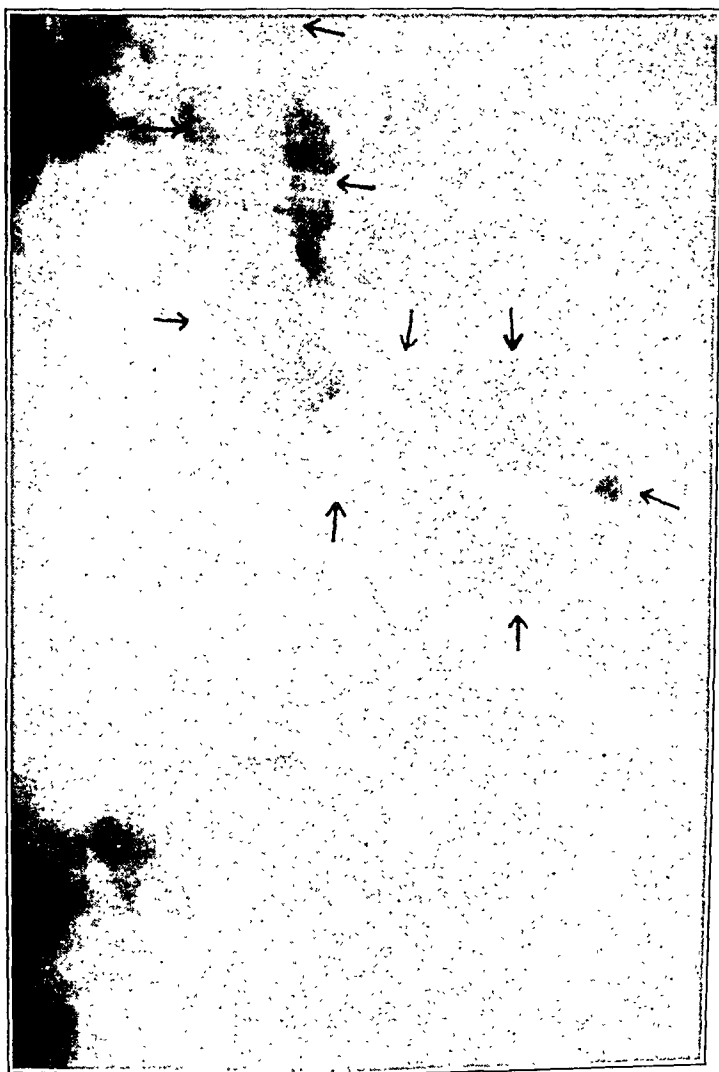


Fig. 2.—Roentgenogram showing double balloon tube in place.

6. Rowntree, L. G.; Zimmerman, E. F.; Todd, M. H., and Ajac J.: Intra-esophageal Venous Tamponage, *J. A. M. A.* **135**:630 (Nov. 8) 1947.

7. Tocantins, L. M.: The Hemorrhagic Tendency in Congestive Splenomegaly (Banti's Syndrome), *J. A. M. A.* **136**:616 (Feb. 28) 1948.

8. Bixby, E. W., Jr.: Correspondence, *J. A. M. A.* **138**:908 (Nov. 20) 1948.

We have tried the methods recently described by the various authors, but in our hands these proved unsatisfactory, since it was difficult to ascertain and maintain the position of the tube. In several cases the tube passed into the stomach or into the upper reaches of the esophagus.

We have used a plastic tube<sup>9</sup> of the type described by Honor and Smathers,<sup>10</sup> but having four lumens. A Rehfuess tip of sufficiently small size to pass through the nares is incorporated into the end of the largest lumen of about 4 feet (122 cm.) of tubing. Eight inches (20 cm.) above this a balloon of rubber, of the consistency of glove rubber, is tied on. Immediately above this and contiguous with this balloon, an additional balloon made of an entire condom is applied. The two balloons are, of necessity, separately inflatable.

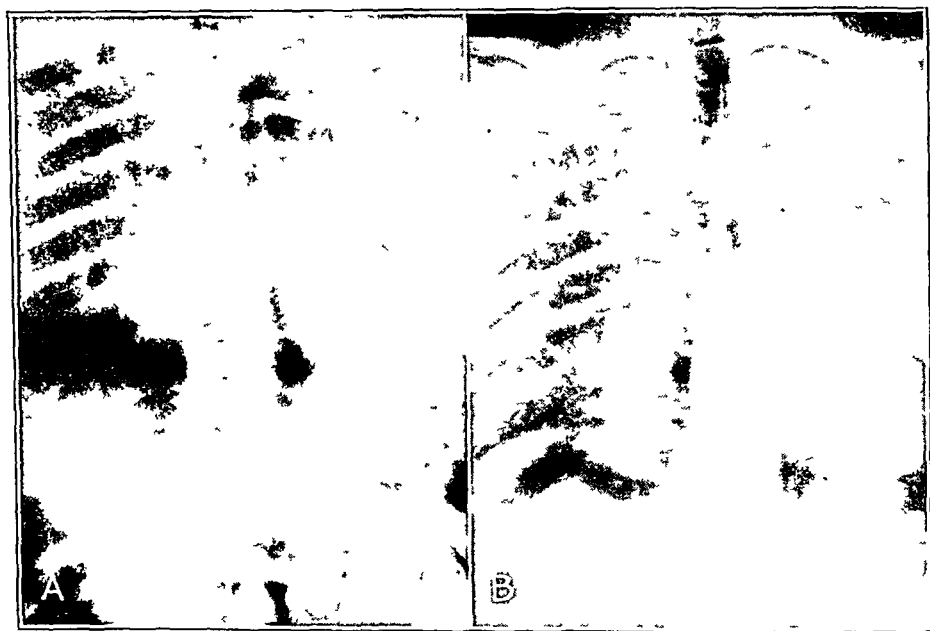


Fig. 3 (case D. S.)—Esophagograms (A) prior to and (B) one month after portacaval shunt.

The tube is passed through the nares and into the stomach, its position being proved by aspiration. The lower balloon is then inflated to such a degree as to give a diameter of  $2\frac{1}{2}$  to 3 inches (6.4 to 7.6 cm.), the tube is pulled up so that the balloon engages snugly at the cardia, which acts as an anchor on the gastric side. The tube is then taped to the nose and the upper balloon is inflated with 200 to 250 cc. of air. The tube is left in place for twelve hours with constant suction

9. Supplied by Payette and Henning, 2238 Second Street, Wyandotte, Mich

10. Honor, W. H., and Smathers, H. M.: A Double-Lumened Plastic Tube for Intestinal Intubation, *Arch Surg.* 55:498 (Oct) 1947.



within the stomach. The upper balloon is deflated after the twelve hour period, and if there is evidence of bleeding it is again inflated and left in place for an additional twelve hours.

The third small lumen may be used for the administration of thrombin<sup>11</sup> after the method of Daly,<sup>12</sup> the thrombin being introduced just above the upper balloon.

After the arbitrary period of twelve hours has elapsed, it has been our practice to deflate the balloons; if bleeding has stopped, material aspirated from the stomach will be free of blood. The tube, however, is left in place. The patient is started on sips of fluid and is gradually placed on a full diet about the third day. Supportive treatment also must be carried out during the procedure.

We have used the tube successfully in 6 cases and have had 2 failures; 1 was in the case of a moribund patient in which the balloons were not checked to see that they were adequately inflated. In the other case at final examination the patient was found to have a bleeding duodenal ulcer.

Following is an illustrative case.

D. S., a 25 year old white man first vomited blood in May 1946. A diagnosis of Banti's disease was made and splenectomy with ligation of coronary veins performed in August 1946. He was well until October 1948, when he vomited blood. Bleeding was controlled by means of the double balloon tube, and a portacaval shunt was performed in November 1948; follow-up in February 1949 revealed that the patient was well, was working at his former job and had gained 30 pounds (9.1 Kg.).

#### SUMMARY

1. A quadruple-lumened plastic tube with two inflatable balloons is presented as a means of control of hemorrhage from esophageal varices.

2. A total of 8 patients have been treated, with 2 failures.

ADDENDUM.—Since the presentation of this paper, we have been informed by a personal communication from Dr. A. H. Blakemore that he has used tamponade successfully as a means of control of bleeding esophageal varices prior to the elective shunt procedure.

Dr William H. Honor assisted in this study and gave technical advice.

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11. Warner, E. D.; Brinkhous, K. M.; Seegers, W. H., and Smith, H. P.: Further Experience with the use of Thrombin as a Hemostatic Agent, *Proc. Soc. Exper. Biol. & Med.* **41**:655 (June) 1939.

12. Daly, B. M.: Use of Buffer Thrombin in the Treatment of Gastric Hemorrhage, *Arch. Surg.* **55**:208 (Aug.) 1947.

## EXPERIENCES WITH ISLET CELL TUMORS

ROY D. McCLURE, M.D.

AND

BROCK E. BRUSH, M.D.

DETROIT

IN 1924, just two years after the discovery of insulin by Banting and Best,<sup>1</sup> Harris<sup>2</sup> published his report on "Hyperinsulinism and Dysinsulinism," having noted in several patients a clinical picture similar to that caused by overdosage of insulin. Nicholls,<sup>3</sup> in 1902, first described the finding at autopsy of an islet cell tumor, but the possible clinical significance was not recognized until this syndrome simulating insulin shock was described by Harris. In 1926 Warren<sup>4</sup> reviewed 20 cases of islet cell hypertrophy observed at autopsy, in only a few of which were there significant symptoms of hyperinsulinism. According to Bockus,<sup>5</sup> an estimated 80 per cent of proved cases of islet cell tumors are clinically silent lesions, giving no symptoms of hyperinsulinism. The first case in which operation was done for an islet tumor was reported by Wilder, Allan, Power and Robertson<sup>6</sup> in 1927. An extensive islet cell carcinoma with metastases was found, and the patient survived only a few weeks. The first successful removal of an islet cell tumor for hyperinsulinism was performed in 1929 by Roscoe Graham, reported by Howland, Campbell, Maltby

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From the Department of General Surgery, Henry Ford Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 18, 1949.

1. Banting, F. G., and Best, C. H.: Internal Secretions of the Pancreas, *J. Lab. & Clin. Med.* **7**:251, 1922. Banting, F. G.; Best, C. H., and others: Pancreatic Extracts in the Treatment of Diabetes Mellitus, *Canad. M. A. J.* **12**:141, 1922.

2. Harris, S.: Hyperinsulinism and Dysinsulinism, *J. A. M. A.* **82**:729 (Sept. 6) 1924.

3. Nicholls, A. G.: Simple Adenoma of the Pancreas Arising from an Island of Langerhans, *J. M. Research* **8**:385, 1902.

4. Warren, S.: Adenomas of the Islets of Langerhans, *Am. J. Path.* **2**:335, 1926.

5. Bockus, H. L.: *Gastroenterology*, Philadelphia, W. B. Saunders Company, 1946.

6. Wilder, R. M.; Allan, F. N.; Power, M. J., and Robertson; H. E.: Carcinoma of the Islands of the Pancreas: Hyperinsulinism and Hyperglycemia, *J. A. M. A.* **89**:348 (July 30) 1927.

and Robinson,<sup>7</sup> and this patient is alive and well today. Approximately 140 patients with islet cell tumor have been operated on, and in another 50 the tumors have been found at autopsy examinations. Whipple<sup>8</sup> has had by far the largest experience, having personally operated on over 25 of these patients.

#### CLINICAL FEATURES

The syndrome of hyperinsulinism may be varied in its manifestations, and also the "attacks" or "spells" vary widely in severity in the same patient. Mild manifestations, marked by fatigue and exhaustion, may exist a considerable length of time before severe attacks of convulsion or loss of consciousness occur. The symptoms usually include weakness, sweating, hunger, paresthesias, pallor, dizziness, palpitation, inability to move the extremities and perhaps syncope. Much of this picture may be caused by the release of epinephrine in an attempt to elevate the blood sugar level. Wilder<sup>9</sup> has grouped the symptoms under those related to the central nervous system, those related to the autonomic nervous system and, finally, the psychic disturbances.

#### DIAGNOSIS

It must be strongly emphasized that spontaneous hypoglycemia is by no means pathognomonic of an islet cell tumor. Since hypoglycemia is a common condition and hyperinsulinism is rather rare, great care must be exercised in the diagnosis of an islet cell tumor. Many organs are involved in the maintenance of a normal blood sugar level. The importance of the liver and the pituitary, adrenal and thyroid glands in addition to the pancreas has become recognized, with the result that investigation of hypoglycemic symptoms includes studies of these various organs. An etiologic classification of spontaneous hypoglycemia proposed by Conn<sup>10</sup> includes the various conditions which must be considered. Insistence on the presence of the "Whipple triad"<sup>8</sup> as an indication for surgical intervention will result in the finding of a tumor in a large percentage of cases. This triad includes nervous system disorders, such as confusion, coma, convulsions or collapse, coming on in the fasting state, accompanied with a blood sugar level of 50 mg.

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7. Howland, G.; Campbell, W. R.; Maltby, E. J., and Robinson, W. L.: *Dysinsulinism, Convulsions and Coma Due to Islet Cell Tumor of the Pancreas, with Operation and Cure*, J. A. M. A. **93**:674 (Aug. 31) 1929.

8. Whipple, A. O.: *Hyperinsulinism in Relation to Pancreatic Tumors*, Surgery **16**:289, 1944.

9. Wilder, R.: *Clinical Diabetes and Hyperinsulinism*, Philadelphia, W. B. Saunders Company, 1941.

10. Conn, J. W.: *The Spontaneous Hypoglycemia*, J. A. M. A. **115**:1169 (Nov. 16) 1940.

or less per hundred cubic centimeters and relief of these symptoms by the administration of glucose. Repeated fasting blood sugar values of 50 mg. or less when the patient is on a normal diet are fairly conclusive. We<sup>11</sup> have felt that glucose tolerance and phosphorus curves are of considerable diagnostic aid if a proper preparatory diet has been used prior to the tests.

#### PATHOLOGY

A certain number of islet tumors have had malignant characteristics microscopically, yet their clinical course has been that of a benign condition. This fact has led Frantz<sup>12</sup> to classify them as benign, malignant and questionable. In 1940 Frantz reported 8 cases of questionably malignant tumors from Whipple's series and collected 16 others in which there was no return of symptoms after many years. Perhaps some of the cases reported by Allan and Marshall<sup>13</sup> in which the tumors were diagnosed as of low grade malignancy by Warren fall into this category. Only about 15 cases of unquestioned malignant islet cell tumors in which metastases to the lymph nodes or liver have occurred have been reported. Marble and McKittrick<sup>14</sup> reported 1 such case in their group of 6 cases of islet cell tumors.

#### SURGICAL TREATMENT

Since in about 15 per cent of the reported cases islet cell tumors have been found to be multiple, careful exploration and palpation of every part of the pancreas is of great importance. If a very careful search of the complete organ does not reveal a tumor, a subtotal pancreatectomy should be performed, with removal of at least four fifths of the gland. Removal of a small portion of the gland in such cases has given uniformly poor results, but subtotal resection has given excellent results in cases reported by Graham,<sup>15</sup> David,<sup>16</sup> Womack<sup>17</sup> and us.<sup>11</sup> According to Duff,<sup>18</sup> tumors which produce the hypoglycemic syndrome

11. Brush, B. E., and McClure, R. D.: Hyperinsulinism Treated by Subtotal Pancreatectomy, *Ann. Surg.* **120**:750, 1944.

12. Frantz, V. K.: Tumors of the Islet Cells with Hyperinsulinism; Benign, Malignant and Questionable, *Ann. Surg.* **112**:161, 1940.

13. Allan, F. N., and Marshall, S. F.: The Surgical Treatment of Islet Tumors of the Pancreas with Hyperinsulinism, *S. Clin. North America* **25**:719, 1945.

14. Marble, A., and McKittrick, L. S.: Islet Cell Tumors of the Pancreas with Hyperinsulinism, *New England J. Med.* **235**:637, 1946.

15. Graham, E. A., and Hartman, A. F.: Subtotal Resection of the Pancreas for Hypoglycemia, *Surg., Gynec. & Obst.* **59**:474 (Sept.) 1934.

16. David, V.: The Indications and Results of Pancreatectomy for Hypoglycemia, *Surgery* **8**:212, 1940.

17. Womack, N.: Hypoglycemia, *Surgery* **2**:793, 1937.

18. Duff, G. L.: Pathology of Islet Cell Tumors of the Pancreas, *Am. J. M. Sc.* **203**:437, 1942.

are usually always over 1 cm. in diameter, yet in many cases they are difficult to detect, as evidenced by the number of tumors missed at the first operation and found later when symptoms persisted. Priestley, Comfort and Radcliffe<sup>10</sup> reported a successful total pancreatectomy for a very small tumor which could not be seen or palpated but was found on pathologic sectioning of the gland.

When a tumor has been completely removed, the clinical results are always excellent, and when such a result is not obtained one must seriously consider the probability that a second tumor has been overlooked at the time of operation either in the pancreas or possibly in some ectopic pancreatic tissue.

#### REPORT OF CASES

The essential features of our 5 cases of hyperinsulinism are presented. Three of these cases have been reported previously elsewhere.<sup>20</sup>

CASE 1.—M. B., a white woman, age 19, was first seen April 11, 1935. Her chief complaints were severe headaches and abdominal cramps. Fasting blood sugar levels were 78 and 99 mg. per hundred cubic centimeters.

In January 1936, the patient complained of frequent attacks of weakness, sweating, tremor and a mental reaction described as stuporous. These attacks were relieved by the ingestion of carbohydrate. A glucose tolerance test revealed that the glucose was utilized rapidly, with a fall to 43 mg. per hundred cubic centimeters in ninety minutes. At operation, Feb. 10, 1936, a tumor was not found and a subtotal pancreatectomy was done. The patient is alive and well today and utilizes glucose normally.

CASE 2.—M. C., a white woman aged 43, was first seen in August 1942, with the complaint of attacks of nervousness, weakness, sweating and hunger, occurring about three hours after eating. These attacks were made worse by exercise and relieved by eating. After a trial on a high protein, low carbohydrate diet, the patient was operated on April 22, 1943. No discrete tumor was found, and a subtotal pancreatectomy was performed. The patient has had no return of symptoms and has normal glucose tolerance.

CASE 3.—G. Y., a white woman aged 40, was first seen on Nov. 13, 1946, complaining of attacks of weakness, blurred vision, slurred speech, profuse sweating and, if not aborted by the ingestion of carbohydrate, syncope lasting from one-half hour to two hours. These attacks had begun two years before and had become progressively worse. The patient was 5 feet 8 inches (173 cm.) in height and weighed 230 pounds (104.3 Kg.); the excess weight had been gained largely in the preceding two years.

Results of liver function tests were normal; the basal metabolic rate was —13 per cent, and a series of determinations of fasting blood sugar averaged 47 mg. per hundred cubic centimeters. Oral and intravenous glucose tolerance tests were completed with difficulty because of hypoglycemic reactions. The intra-

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19. Priestley, J. T.; Comfort, M. W., and Radcliffe, J.: Total Pancreatectomy for Hyperinsulinism Due to an Islet Cell Adenoma, *Ann. Surg.* **119**:211, 1944.

20. (a) Brush and McClure.<sup>11</sup> (b) Kuffel, M. J.; Foster, D. P., and Lowrie, W. L.: Hyperinsulinism with Hypoglycemia Relieved by Removal of Pancreatic Tumor, *Am. J. Digest. Dis.* **14**:279, 1947.

venous test curve showed a level of 34 mg. per hundred cubic centimeters one and one-half hours after the administration of glucose and 44 mg. at five hours. At operation a nodule 2 cm. in diameter was removed from the head of the pancreas. The patient thereafter lost weight, and her blood sugar level returned to normal with relief of the symptoms.

CASE 4.—J. P., a white woman aged 28, first seen April 15, 1947, complained of spells of "loss of awareness of her surroundings," incoherence, numbness in the extremities, face and lips and perspiration. These frequently came on in the morning before breakfast and were often accompanied with headaches. Relief from ingestion of carbohydrates was dramatic. Blood sugar levels during attacks

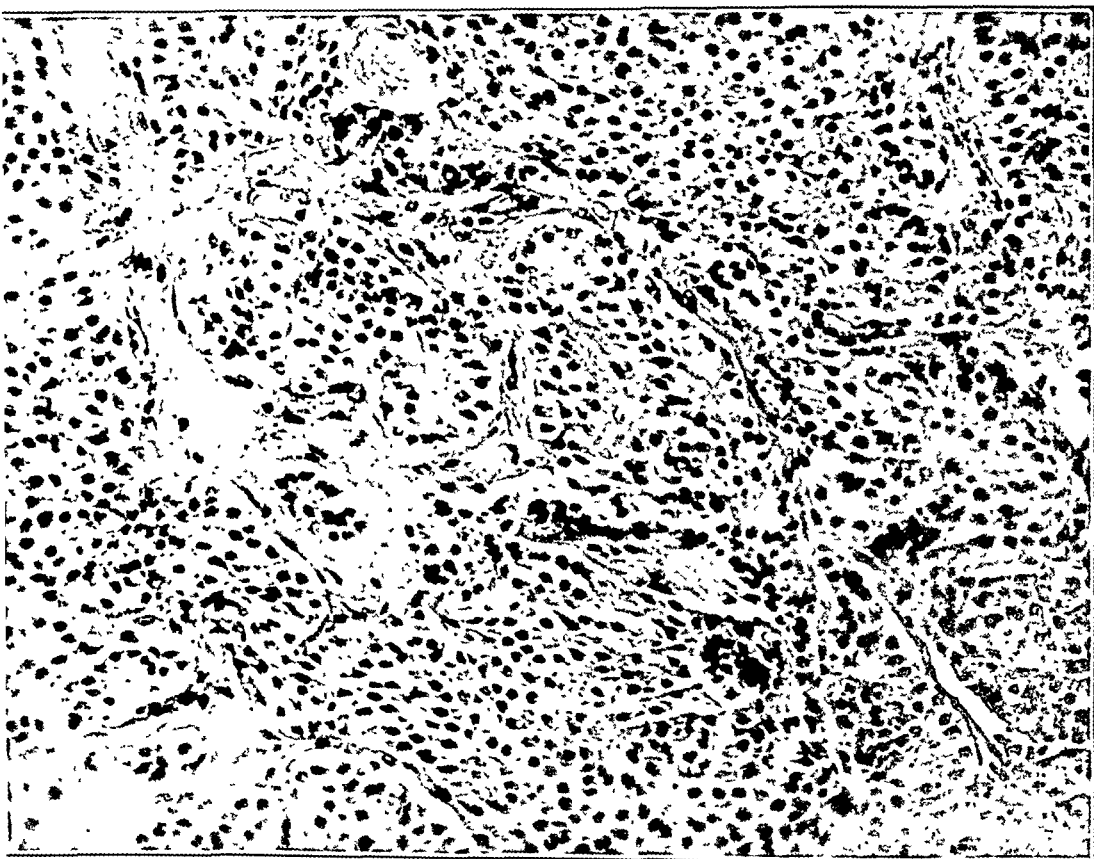


Fig. 1 (case 4).—Islet cell adenoma.

ranged from 32 to 37 mg. per hundred cubic centimeters. The basal metabolic rate was  $-2$  per cent. Results of liver function tests were normal, as was the electroencephalogram; stereoroentgenograms of the skull revealed no abnormalities. At operation, on June 6, 1947, an islet cell adenoma 1.5 cm. in diameter was removed from the head of the pancreas (fig. 1). In May 1948 an epigastric swelling appeared, and a pseudocyst of the pancreas was diagnosed. On June 2, 1948, 400 cc. of material was aspirated and the cyst marsupialized. After six weeks small amounts of sodium morrhuate were instilled, and complete healing occurred three weeks later. The patient has had no return of symptoms from the adenoma or the cyst, and her blood sugar levels are within normal limits.

CASE 5:—H. J., a white man aged 45 years, was first seen in June 1947, complaining of attacks of dizziness, staggering, disorientation, weakness and collapse. These attacks had begun only six months previously and had become progressively worse. Carbohydrate relieved the symptoms. Blood sugar levels during the attacks ranged from 35 to 45 mg. per hundred cubic centimeters, and the tolerance curve was flat. A roentgenogram showed narrowing of the second portion of the duodenum.

At operation, on July 12, 1947, a large encapsulated tumor was noted along the upper border of the pancreas in the region of the neck. The tumor was removed. It weighed 50 Gm. and on microscopic section proved to be an adeno-

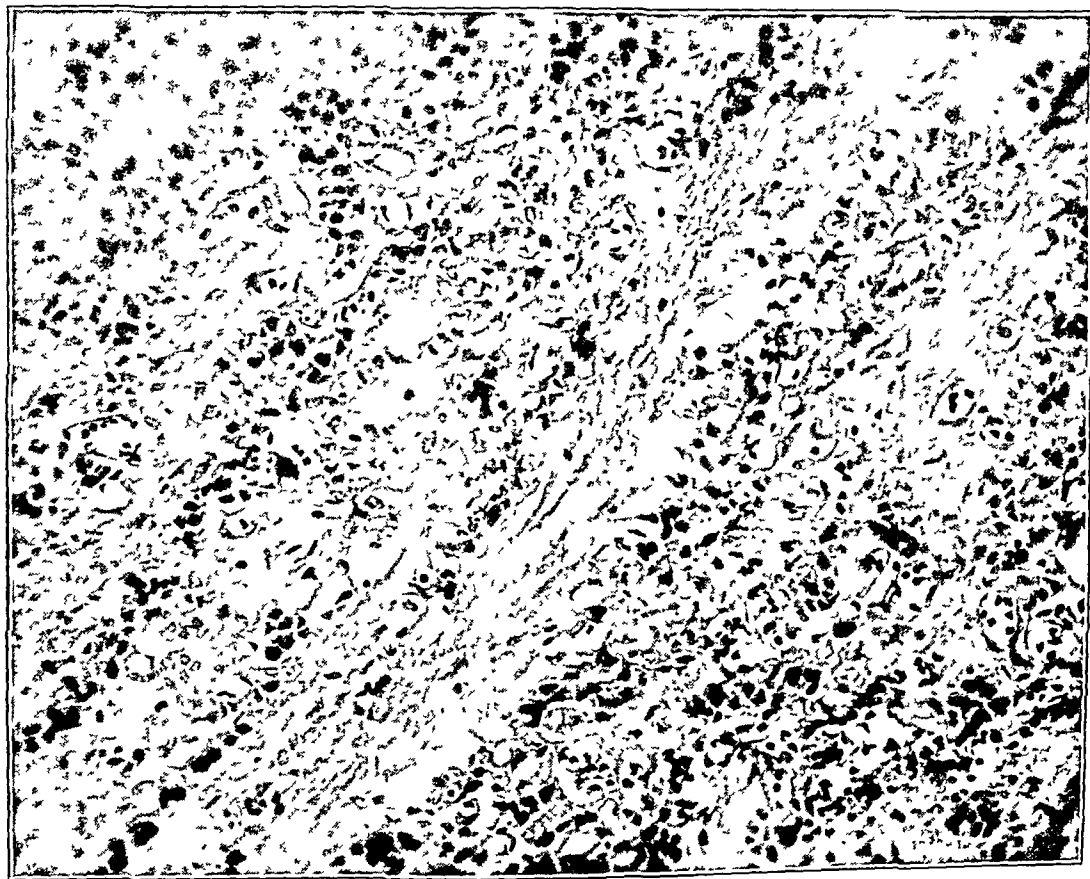


Fig. 2 (case 5).—Islet cell carcinoma.

carcinoma (fig. 2). A large lymph node in the gastrohepatic mesentery was removed, and it was found that the normal tissue had been completely replaced by tumor tissue. Because of the failure to recur in many of cases of tumor of low grade or suspected malignancy and the definite encapsulation of this tumor, it was thought that possibly after wide excision of the tumor and the involved lymph nodes cure might be obtained. However, the symptoms of hyperinsulinism gradually returned, and, in view of the disappointing results of alloxan therapy, a more radical operation was undertaken. A total pancreatectomy was performed on July 14, 1948 with great difficulty because of the extension of the growth. The patient died on the fifth postoperative day.

## COMMENT

Our 5 cases represent the three situations that may be found at operation: no discernible tumor, an islet adenoma and an islet cell carcinoma. In the 2 cases in which a tumor was not found and a subtotal resection was performed and in the 2 cases in which a benign adenoma was found and removed, equally good clinical results were obtained. In the case of carcinoma with metastases there was recurrence of the tumor, as there has been in all other reported cases. The development of a pancreatic cyst, which occurred in 1 case, is a fairly common complication encountered in operation on the pancreas and is usually handled very well by marsupialization.

In most instances the pancreas can best be completely examined by an approach through the gastrocolic omentum; however, in 2 of our cases the tumor was removed by incising the gastrohepatic omentum and employing downward traction on the stomach. The importance of frequent determinations of blood sugar levels in the immediate post-operative period as a guide for management has been sufficiently stressed.

## SUMMARY

Five cases of hyperinsulinism are reported. In 2 cases a benign tumor was found; in 2 tumor was not found, but an excellent result was obtained by subtotal resection of the pancreas. In 1 case there was carcinoma with metastases to the lymph nodes, with recurrence after resection of all visible and palpable diseased tissue.

The criteria for a diagnosis of an islet cell tumor are stressed, as is the importance of operation when these features are present. The necessity for a careful exploration of the total gland at operation is likewise stressed.



## APPENDICITIS

A Ten Year Survey: 1935 Through 1944

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APPENDICITIS is still a very prevalent disease, and there are still many problems in the treatment which have not been conclusively solved. The accumulation and the reporting of the experience in the treatment of adequately large groups of patients will record the trend of thought and management as well as assist in forming conclusions helpful in the treatment of appendicitis. It is for that purpose that this report is made concerning the treatment of appendicitis in St. Joseph's Mercy Hospital, Ann Arbor, Mich., during the ten year period 1935 through 1944. This period was chosen because the first five years represent the introduction of intravenous fluids, continuous gastric suction, more frequent blood transfusions and certain changes in surgical technic. The second five years had the added advantages of the sulfonamide compounds, but penicillin was not yet used. These two periods lend themselves to certain comparisons as to methods of treatment and results.

In this study are included the cases of all patients treated for appendicitis or for whom appendectomy was done as a primary operation during this ten year period. Any statistical study is as reliable as the records on which it is based. For this purpose, it is fortunate that St. Joseph's Mercy Hospital has a closed staff. Although a total of nineteen surgeons performed appendectomies during this ten year period, six did 95 per cent of the total operations and three of these did 75 per cent of the total. Operative notes were dictated by the operating surgeon, and the records have been well kept, except during 1944, when the war curtailed the staff. The attitude of the staff has been one of conservatism toward innovations. Unfortunately, during 1935 through 1937, there were still some patients who were being treated without the benefit of intravenous fluids and gastric suction. Sulfonamide compounds were little used before 1941. Early ambulation was not practiced during the period studied. Changes were adopted only when proved by experience elsewhere. The vast majority of the patients treated came from the

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immediate vicinity and must be considered as private patients, although occasionally their care was financed by the county welfare funds.

During the ten year period of study (1935 through 1944) 2,179 patients were treated for appendicitis. This comprised 4 per cent of all patients admitted during this period, and the operations constituted 8 per cent of all major surgical procedures.<sup>1</sup> Of the total group, 913, or 41 per cent, were classified as having recurrent or interval appendicitis, and they will not be referred to again in this paper, except in the matter of correlating the clinical problem with the pathologic findings. There was no mortality in that group. A group of 1,266 patients were treated for suppurative appendicitis, with an over-all mortality of 1.9 per cent; but, of these, 225 either had no microscopic evidence of suppurative appendicitis or had another disease which was found at operation. There were 2 fatalities. This leaves 1,042 patients treated correctly for suppurative appendicitis, with an over-all mortality of 2.1 per cent. In the discussion of treatment, the mortality statistics will be adjusted to

TABLE 1.—*Classification of 2,179 Cases of Appendicitis in Which Treatment Was Given: 1935-1944*

Classification	Cases		Mortality, %
	No.	%	
Recurrent appendicitis.....	913	41.9	0
Suppurative appendicitis.....	1,042	47.7	2.1
Unsubstantiated diagnosis.....	225	10.0	0.1

eliminate figures for patients who received no treatment, owing either to their critical condition or to an error in diagnosis.

All operative material was examined by the pathologist. The terminology of the pathologist may be misleadingly polite, or he may honestly wish to admit that there may be clinical symptoms unexplained by microscopic changes. Because there may be described microscopically in an appendix many changes which must be interpreted with caution in view of the expected wear and tear of time, for the purpose of this paper only those with the minimum criterion of acute suppurative appendicitis with purulent exudate in the lumen and pyogenic infiltration of the wall were included under the heading of acute appendicitis. This eliminated cases of the sort reported as catarrhal appendicitis, active chronic appendicitis, acute exacerbation of chronic appendicitis, mechanical appendicitis and others. These cases were placed in the group of interval or recurrent appendicitis. This is a very rigid classification and undoubtedly helps to account for a high percentage of error in diagnosis. However, it places the cases included in this report beyond

1. McCullough, J. Y.: Survey of Some Aspects of Appendicitis, *Ann. Surg.* 75:453 (March 4) 1948.

question. A combination of the clinical picture presented by the patient, the operative findings described by the surgeon and the report of the pathologist was used to make the diagnosis of appendical abscess or peritonitis of appendical origin. Most authors<sup>2</sup> classify their reported cases as instances of (1) simple acute appendicitis, (2) peritonitis of appendical origin and (3) appendical abscess. Only a few authors<sup>3</sup> have expressed the belief that it is possible to separate the cases of localized peritonitis from those of generalized or spreading peritonitis. During the period studied by this report, the staff of this hospital thought that the clinical picture of generalized peritonitis was clearcut enough to warrant that diagnosis. Spreading peritonitis, indicating a progressive condition, was a diagnosis made only after the clinical course of the patient showed it to be so. The observations of the pathologist have occasionally been used as the basis for classification.<sup>4</sup>

In the detailed discussion of treatment, localized peritonitis of appendical origin will be differentiated from generalized peritonitis,

TABLE 2.—*Classification of 1,042 Cases of Proved Appendicitis: 1935-1944*

Classification	Cases		Mortality, %
	No.	%	
Acute appendicitis.....	771	73.9	0.1
Appendical peritonitis.....	219	21.0	7.3
Appendical abscess.....	52	4.9	9.6

but for general purposes of discussion the 1,042 cases are classified as follows (table 2): (1) 771 cases of acute appendicitis in which the disease was localized to the appendix; (2) 219 cases of appendical peritonitis in which at operation there were cloudy fluid and purulent exudate on the surrounding organs or in which the clinical picture was that of a severely ill patient, giving a history compatible with appendicitis and presenting the signs of generalized peritonitis, and (3) 52 cases of appendical abscess.

2. (a) Reid, M. R.; Poer, D. H., and Merrell, P.: A Statistical Study of 2,921 Cases of Appendicitis, *J. A. M. A.* **106**:665 (Feb. 29) 1936. (b) Miller, E. M.; Fell, E. H.; Brook, C., and Todd, M. C.: Acute Appendicitis in Children, *J. A. M. A.* **115**:1239 (Oct. 12) 1940. (c) Green, H. W., and Watkins, R. M.: Appendicitis in Cleveland, Surg., Gynec. & Obst. **83**:613 (Nov.) 1946. (d) Meyer, K. A.; Requarth, W. P., and Kozoll, D. D.: Progress in the Treatment of Acute Appendicitis, *Am. J. Surg.* **72**:830 (Dec.) 1946. (e) Hoerr, S.: Factors in the Reduction of Mortality of Appendicitis, *Surgery* **22**:402 (Aug.) 1947. (f) Strohl, E. L., and Sarver, F. E.: Acute Appendicitis, *Arch. Surg.* **55**:530 (Nov.) 1947.

3. (a) Barrow, W., and Ochsner, A.: Treatment of Appendical Peritonitis, *J. A. M. A.* **115**:1246 (Oct. 12) 1940. (b) Ochsner, A., and Johnston, J. H.: Appendical Peritonitis, *Surgery* **17**:873 (June) 1945.

4. Jennings, J.; Burger, H., and Jacobi, M.: Acute Appendicitis: A Clinical and Pathological Study of 1,630 Cases, *Arch. Surg.* **44**:896 (May) 1942.

There have been many series of cases reported in the literature.<sup>5</sup> Up to the middle 1930's, there was a slow, but steady, decrease in the mortality from appendicitis. In the last ten years, there has been a sharp decrease in the mortality. The possible variables have been carefully analyzed many times to find the secret of success, but usually it has been hard to credit any one factor.<sup>6</sup> However, early diagnosis and immediate operation obviously constitute the potential factors making for a perfect record, as the mortality in the first twenty-four hours of the disease is negligible. If there is a significant reduction in the time before operation and therefore in the percentage of complicated cases, an improvement in the mortality may be expected. Also, the role of the sulfonamide compounds and penicillin may be important.

TABLE 3.—*Variation in Annual Distribution and Mortality*

Year	Acute Appendicitis		Appendicitis with Localized Peritonitis		Appendicitis with Generalized Peritonitis		Abscess		Totals		
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	%
1935.....	36	0	19	0	0	0	3	3	58	2	3.4
1936.....	48	1	15	3	2	1	2	0	67	5	7.4
1937.....	65	0	11	0	0	0	7	1	83	1	1.2
1938.....	89	0	16	1	2	0	5	2	112	1	0.8
1939.....	70	0	16	0	5	1	7	0	98	3	3.0
1940.....	98	0	30	3	2	0	6	0	136	3	2.2
1941.....	111	0	18	0	3	0	3	0	135	0	0.0
1942.....	123	0	21	1	7	2	5	0	156	3	1.9
1943.....	80	0	21	1	6	3	5	0	112	4	3.5
1944.....	51	0	22	0	3	0	9	0	85	0	0.0
Total.....	771	1	189	9	30	7	52	5	1,042	22	
Mortality.....	0.1%		4.7%		23.3%		9.6%		2.1%		

It must be remembered that the improvement was being noted before sulfonamide drugs were used. Before I present my impressions of the significance of early diagnosis, short time interval before operation, age, incisions, drainage and the sulfonamide drugs, it would be well to consider the variations in annual distribution and mortality (table 3). It can be seen that near perfection was achieved during 1937 and 1938; hence a report based on these two years would have been optimistic. Also, in 1941 there were 135 consecutive cases without a death; actually, 175 cases were observed before a death occurred, during 1942. This

5. Schullinger, R.: Observations on Mortality from Acute Appendicitis at a University Hospital, 1916-1946, *Ann. Surg.* **126**:448 (Oct.) 1947. Jennings, Burger and Jacobi.<sup>4</sup>

6. (a) Hoerr, S.: Mortality Factors in Acute Appendicitis, *Surgery* **18**:205 (Sept.) 1945. (b) Zinninger, M., and Taskiro, S.: Appendicitis: A Review of Nine Hundred and Thirty-Six Cases at the Cincinnati General Hospital, *Arch. Surg.* **53**:545 (Nov.) 1946. (c) Green and Watkins.<sup>2c</sup> (d) Meyer, Requarth and Kozoll.<sup>2d</sup> (e) Hoerr.<sup>2e</sup>

fact is mentioned to emphasize the weakness of any conclusion based on a yearly report.

#### DELAY IN HOSPITALIZATION

Delay in hospitalization, or the time interval from the recorded onset of symptoms to admission to the hospital, has frequently been emphasized. As many authors have pointed out, if the operation occurs before the disease has extended beyond the appendix the mortality will be negligible. Statistical analyses giving the average number of hours before admission are of interest and have been used as an indication for operation or conservative treatment.<sup>3a, b</sup> If a significant reduction has been made, progress is undoubtedly being made, but the truly important factor is: In what stage of the disease was the patient admitted to the hospital? If there is a significant reduction in the number of complicated cases, the mortality will fall. Unfortunately, as many authors<sup>7</sup> have pointed out, peritonitis may occur very quickly in the clinical course of the disease. There was no improvement to report in the two five year periods studied. During the years 1935 to 1939, 26.1 per cent of the patients had evidence of peritonitis or abscess and 25.9 per cent during 1940 to 1944. Almost half of the cases of localized peritonitis and a third of the cases of generalized peritonitis occurred within twenty-four hours of the recorded onset of symptoms. However, it is significant to note that no deaths occurred in patients operated on within twenty-four hours of the onset of symptoms. Among those operated on from twenty-four to forty-eight hours after the onset of symptoms there was a 4.4 per cent mortality and an 8.4 per cent mortality among those operated on after three days.

#### PROBLEMS OF DIAGNOSIS

The relative importance of the various symptoms, physical signs and laboratory data in the diagnosis of appendicitis has been described many times. There would seem to be no reason for an error in diagnosis or delay in treatment once the patient has reached the hospital. Unfortunately, this is not so. In addition to those rare cases in which the diagnosis is not made until late in the disease or until autopsy, there is a significant group in which the diagnosis is in doubt on admission and may still be in doubt at operation. Zininger<sup>6b</sup> found only 61 per cent of patients presented the classic picture of appendicitis. In this series 92 per cent of patients with proved acute appendicitis had either a reasonably typical history or physical findings. Operation was delayed in 6.2 per cent for further study with no recorded detriment to the patient. Of 189 cases of localized appendical peritonitis, operation was delayed in 6.8 per cent for further study, with probable detriment to 3 patients; this delay may have been a contributing factor to the death of another. A

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7. Jennings, Burger and Jacobi.<sup>4</sup> Zininger and Taskiro.<sup>6b</sup>

delay of several hours in an atypical case for a second examination, recheck of the laboratory work or consultation will seldom do harm and may prevent unnecessary operations. This attitude in no way excuses the missed diagnosis. However, the benefits of immediate operation have been so emphasized that in some communities, the patient need only mention discomfort in the right side to find himself the victim of an emergency operation. Granted that there is no excuse for delaying an operation that is indicated, it would still be a good thing if at hospital staff meetings the report of the pathologist could be checked for all appendixes removed at an emergency operation. As previously mentioned, the correlation of the clinical picture and the findings of the pathologist is still to be clarified. Jennings, Burger and Jacobi<sup>4</sup> have shown that there is little correlation between the clinical signs and symptoms and the pathologist's findings. They report perforation after only six hours of illness. In this series, we have taken acute suppurative appendicitis with purulent exudate in the lumen and pyogenic cellular infiltration of the wall as the minimal criterion for the clinical diagnosis of acute appendicitis. This is a very rigid classification and, perhaps, should be considered in the error in diagnosis. Of 1,229 patients operated on for suppurative appendicitis, 187 did not have the microscopic evidence previously mentioned. Of these 187 patients 149 were operated on as presenting true emergencies and 38 only after delay for study. Eighty-one per cent of these gave either a satisfactory history or had physical findings typical of appendicitis. There was 1 fatality, the patient dying with the signs and symptoms of generalized peritonitis on the fourth postoperative day. Either the pathologist reported on the wrong appendix and this was a true case of suppurative appendicitis, or the stump, which had been buried, blew out. These 187 cases represent a 15 per cent error in diagnosis of acute appendicitis, which was fairly evenly distributed among the six surgeons doing 75 per cent of the operations. Perhaps this error is too high; however, this figure is not far from that of Jennings and associates,<sup>4</sup> who found 11.9 per cent unsubstantiated diagnoses. Furthermore, of considerable interest is the fact that of the 994 patients operated on for recurrent appendicitis, 81 had acute suppurative appendicitis. This was an 8 per cent error and probably only helps to confuse the problem in the correlation of the clinical picture with the observations of the pathologist. There was no significant difference in the two five year periods studied.

The differential diagnosis between acute appendicitis and other abdominal conditions has been outlined many times. However, as is shown in table 4, other abdominal diseases were encountered in patients with a preoperative diagnosis of acute appendicitis.

Mistakes in diagnosis were made for 38 patients, or 3 per cent of those operated on for acute appendicitis. In only 4 instances was opera-

tion mandatory: in the cases of acute Meckel diverticulitis and volvulus of the ileum. More thorough study would certainly have eliminated the operations for genitourinary conditions and for pregnancy. The other 20 patients whose disease originated in the pelvis, theoretically should not have been operated on; but, practically, this is probably not a bad range of error. There were no significant differences in the two five year periods. There was 1 fatal case, that of a patient with acute cholecystitis whose gallbladder was drained. Death occurred on the sixteenth postoperative day. Autopsy showed only a dilated right side of the heart.

#### INCISIONS

At the beginning of this study the right rectus incision was used almost exclusively. As the advantages of a muscle-splitting incision in the right lower abdominal quadrant were recognized, the right rectus incision was largely discarded, except by one operator. Although this change occurred as the mortality was being lowered, the improvement

TABLE 4.—*Classification of 38 Cases not Acute Appendicitis*

Pelvic	Genitourinary	Gastrointestinal	Miscellaneous
Ruptured follicle.... 11	Urinary tract	Meckel's diverticu-	Toxic psychosis.. 1
Acute salpingitis.... 8	infection..... 4	litis..... 3	Peritonitis
Chronic salpingitis. 1	Sulfonamide	Acute cholecystitis... 3	following
Pregnancy..... 2	crystalluria..... 1	Volvulus of ileum.... 1	chickenpox.... 1
	Hydronephrosis.... 1		
	Perirenal abscess.... 1		
Total..... 22	7	7	2

took place among the complicated cases, in which there were other factors, probably of more importance than the incision. Despite the benefits credited to the McBurney incision by other authors,<sup>8</sup> it is hard to evaluate properly the incision used in this series, except as to morbidity. The right rectus incision was consistently associated with an average hospital stay of fourteen plus days, whereas, in contrast, the McBurney or Davis incision necessitated slightly less than seven days.

#### DRAINAGE

When to drain has always been a controversial point. Schullinger<sup>5</sup> has again repeated the principles of drainage, which are, in short: to drain actual purulent fluid, to drain areas in which there is necrotic tissue and to drain clean areas that have been opened to infection. There has been a marked tendency in recent years not to drain but to let the peritoneal cavity take care of the infection.<sup>9</sup> Certainly the

8. Reid, Poer and Merrell.<sup>2a</sup> Strohl and Sarver.<sup>2f</sup> Jennings, Burger and Jacobi.<sup>4</sup> Schullinger.<sup>5</sup> Zininger and Taskiro.<sup>6b</sup>

9. Jackson, A.: Early Ambulation in Cases of Perforated Appendicitis, Arch. Surg. 54:644 (June) 1947. Meyer, Requarth and Kozoll.<sup>2d</sup>

morbidity is greatly reduced by primary peritoneal closure unless a secondary abscess occurs. Zininger<sup>6b</sup> has warned against too frequent closure, as he found an increase in intra-abdominal abscess in a more recent series of cases reported. In this series, a change of policy occurred suddenly in 1939. Prior to that time drainage was instituted in 18 per cent of the cases of acute appendicitis; subsequently, in only 3 per cent. In 6 cases pelvic abscesses occurred, in 4 despite drainage. Prior to 1939, drainage was instituted in 91 per cent of the cases of localized peritonitis. Subsequently, only 50 per cent, and during the last year of this study, only 33 per cent were drained. One abscess in the right lower quadrant and 1 subphrenic abscess occurred despite the usual type of drainage. One abscess in the right lower quadrant occurred after primary peritoneal closure. All appendical abscesses operated on were drained. This small incidence of secondary intra-abdominal abscess, occurring mainly despite drainage, seems clearly to indicate that the increase of primary peritoneal closure had

TABLE 5.—*Age Distribution*

Years	No. of Cases	% of Complicated Cases	No. of Deaths*	Mortality Rate, %
0-9 .....	76	50	2	2.6
10-49.....	558	15	4	0.4
50-59.....	53	64	6	11.0
60-69.....	31	74	4	12.0
70-79.....	5	100	4	80.0
80 .....	1	100	1	100.0

\* Age unknown for 1 death.

been done without harm to the patient and should continue. Wound drainage alone was frequently done in cases in which there had been contamination of the wound. This was either as a delayed closure technic or as drainage to the peritoneum.

The fact that in all fatal surgical cases drainage had been instituted only indicates the seriousness of the patients' condition rather than discrediting drainage. It also shows that primary peritoneal closure when used did not contribute to the mortality. Drainage will still be used when there is something localized to drain. This will mean appendical abscesses and many cases of peritonitis.

#### AGE

Appendicitis in the very young and in the advanced age group has been shown to carry a high mortality.<sup>4</sup> The symptoms and clinical findings are less typical, and the patients are less able to withstand surgical procedures. Also, peritonitis will have occurred more frequently by the time of operation. In this series, the mortality among the patients over 60 years of age was extremely high (24 per cent),



emphasizing the problem of surgery in the aged. Table 5 shows the age distribution, per cent of complicated cases and mortality. The greatest incidence was in the decade 10 to 19 years (292 cases) and the next greatest in the 20 to 29 year group (256 cases).

There was no significant difference in the age incidence in the two five year periods studied.

#### CONSERVATIVE TREATMENT

As stated earlier in this report, the consensus of this staff has been that the diagnosis of generalized peritonitis can be made in contrast to that of localized peritonitis. The diagnosis of appendical abscess seems to have been more difficult to make. The selection of cases for conservative treatment has depended on the individual surgeon's opinion. Conservative treatment for generalized peritonitis and abscess was started in this hospital in 1938. Since that time, it has had a definite place in the management of these conditions, particularly in the critically ill. However, conclusions drawn from such a small series of cases as this series must be carefully considered.

Of 189 patients with localized peritonitis 187 were operated on; hence conservative treatment was not used. Of 30 patients with generalized peritonitis, the cases of 27 are suitable for study. Two patients died before treatment could be started, and a diagnosis was not made until autopsy in the third case. Of these 27 remaining patients, 13 were operated on, with 3 deaths from peritonitis. Fourteen patients were treated conservatively, with 1 death, that of an elderly patient with diabetes associated with cardiovascular disease who was not considered fit for operation during the sixteen days of his hospital stay.

There were 52 cases of appendical abscess. Fifty only are suitable for study, as 1 patient was considered too ill for any treatment and the diagnosis was not made until autopsy in the second case. Thirty patients were operated on, with 2 deaths. Drainage alone (used in 17 patients, with no deaths) was done unless the appendix was readily available. In 5 cases, the abscess was not suspected preoperatively, and in 2 additional cases, the preoperative diagnosis was that of a pelvic condition. More accurate diagnosis would have reduced the number of persons operated on. Twenty patients were treated conservatively, but 5 subsequently required drainage of the abscess, with 1 fatality. Conservative treatment for generalized peritonitis and appendical abscess was certainly followed by no greater mortality than was immediate operation. Because of the tendency to use conservative treatment for critically ill patients, it should receive more credit in the reduction of the mortality than the statistics would indicate. Although conservative treatment was not used until 1938, statistically it was used equally in the two five year periods.

## THE SULFONAMIDE COMPOUNDS

The sulfonamide compounds were not used until late in 1940 and were not used adequately until 1941. They were never used to any great extent in simple acute appendicitis, the peak of popularity being in 1942 with 10 per cent of the cases. Consistently, 50 per cent of the patients with localized peritonitis have received these drugs since 1940. In the 4 fatal cases suitable for study, 2 patients received adequate sulfonamide therapy, 1 was inadequately treated and 1 received no sulfonamide drugs. Eighty-five per cent of the patients with generalized peritonitis have received these drugs since 1940. Of 3 patients who died, 2 received adequate amounts of sulfonamide compounds and 1 received none. Seventy-seven per cent of the patients with abscess received adequate sulfonamide therapy. There were no deaths.

There have been many reports concerning sulfonamide treatment of appendicitis.<sup>10</sup> Its routine use has been advocated, and much improvement has been credited to its use. However, the routine use of sulfonamides will not eliminate all complications or deaths from appendicitis, and physicians who expect them to do so will certainly be disappointed. For the complicated cases—that is, of abscess and peritonitis—sulfonamide therapy certainly has been accepted. This small series of cases tends to show that sulfonamide compounds will not prevent death from appendicitis but must be given much of the credit for reducing mortality. Penicillin and streptomycin are now being evaluated.

## MORTALITY

The cause of death has been studied carefully by many authors and has been reported in most articles.<sup>11</sup> Peritonitis, ileus and undrained abscesses are the commonest causes. Table 6 shows the causes of death in this series.

Generalized peritonitis is the most common. Of the 10 such cases treated, 9 occurred in the period 1935-1939, which would indicate that postoperative generalized peritonitis has almost been eliminated as a cause of death among patients treated in 1940-1944 and is a major

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10. (a) Ravdin, T.; Rhoades, J., and Lockwood, J.: The Use of Sulfanilamide in the Treatment of Peritonitis Associated with Appendicitis, *Ann. Surg.* **111**:53 (Jan.) 1940. (b) Stafford, C.; Beswick, J., and Debb, P. H.: Evaluation of Sulfonamides in the Treatment of Peritonitis of Appendiceal Origin, *Am. J. Surg.* **64**:227 (May) 1944. (c) Aycok, T., and Farris, E. M.: The Possible Effects of Sulfonamides on the Mortality of Appendicitis, *Ann. Surg.* **121**:710 (May) 1945. (d) Mueller, R.: The Local Use of Sulfonamides in the Treatment of Acute Appendicitis, *Ann. Surg.* **122**:625 (Oct.) 1945. (e) Griffin, W.; Silverstein, H.; Hardt, H., and Seed, L.: Prophylactic Chemotherapy in Appendicitis, *J. A. M. A.* **133**:907 (March 29) 1947.

11. Green and Watkins.<sup>2c</sup> Schullinger.<sup>5</sup> Hoerr.<sup>6a</sup>

factor in the improvement in mortality in this period. There is, of course, no excuse for the failure to make a diagnosis in 2 cases until autopsy or for the postoperative subphrenic abscess, which was allowed to perforate into the lung. Little could have been done to prevent the deaths from coronary occlusion and pulmonary embolism. A more optimistic or energetic attitude might have saved the 4 elderly patients who were considered either too feeble to withstand operation or who were allowed gently to pass on.

In evaluating the effect of treatment on the mortality statistics, it would seem reasonable to eliminate from consideration those patients who received no treatment, either because they were moribund on admission (2 cases) or because no diagnosis was made until autopsy

TABLE 6.—*Causes of Death*

	1935-1939	1940-1944
Generalized peritonitis.....	9	3*
Age and cardiovascular disease.....	1	3
No diagnosis.....	1	1
Undrained subphrenic abscess.....	0	1
Coronary occlusion.....	0	2
Pulmonary embolism.....	0	1

\* 2 patients moribund on admission.

TABLE 7.—*Results of Treatment on Mortality Statistics*

	Acute Appendicitis			Localized Peritonitis			Generalized Peritonitis			Abscess			Totals		
	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%	Cases, No.	Deaths, No.	%
1935-1939	308	1	0.32	77	4	5.2	9	2	22	23	4	17	416	11	2.6
1940-1944	463	0	0.0	112	5	4.4	18	2	11	28	0	0.0	622	7	1.1

(2 cases). The 2 patients with coronary occlusion and the 1 with pulmonary embolism were clinically well at the time of the complication. Autopsy showed a clean abdomen in 2, but these cases are included because the treatment may have influenced the occurrence of the fatal complication. There were no deaths attributed to anesthesia.

Table 7 shows the difference in the mortality statistics in the two five year periods studied, corrected as just outlined. The over-all mortality dropped from 2.6 to 1.1 per cent, which is significant. This was achieved by the great improvement in the results of the treatment of abscess and generalized peritonitis. In attempting to determine the reason for this improvement, the fact that generalized peritonitis was almost eliminated as a cause of death among the treated patients stands out. Undoubtedly, the use of sulfonamide drugs must be given the greatest credit for this change. Although the statistics do not prove it, there is the impression among the staff that conservative treatment has

done much to bring about this improvement. Other factors, such as age distribution, diagnosis, early operation and drainage, were not appreciably different in the two periods. The change from the right rectus incision to the muscle-splitting incision in the right lower quadrant is hard to evaluate. Undoubtedly, there is less chance of converting a localized peritonitis into a generalized peritonitis by the use of the lateral incision.

The results of treatment of appendicitis complicated with localized peritonitis were not encouraging. The sulfonamide compounds were used in only 50 per cent of the cases, but of the 5 deaths only 1 was due to peritonitis. Three were associated with cardiovascular conditions and 1 with faulty diagnosis. Although success may be attained in controlling postoperative peritonitis, further improvement will require more successful treatment of the problems of the aged.

#### CONCLUSIONS

A survey of the treatment of appendicitis at St. Joseph's Mercy Hospital during 1935-1944 has shown an improvement. This was obtained mainly in those cases of appendical abscess and generalized peritonitis treated during the second five year period. The reduction in postoperative generalized peritonitis as a cause of death would indicate that the use of sulfonamide drugs deserves much credit. However, 4 deaths were recorded, despite adequate sulfonamide therapy. Conservative treatment is the second factor which has favorably influenced the results. To improve results still further, more adequate treatment must be directed toward the problem of the aged and more accurate diagnosis must be obtained.

#### SUMMARY

The treatment of appendicitis in St. Joseph's Mercy Hospital, Ann Arbor, Mich., during a ten year period, 1935 to 1944, is reviewed. During this time, 2,179 patients were treated primarily for appendicitis, of whom 41.9 per cent were treated for interval appendicitis, 47.7 per cent for proved suppurative appendicitis and 10.4 per cent with the diagnosis of appendicitis unsubstantiated.

Improvement was noted in the second five year period. The variable factors are reviewed to determine the cause of this improvement. The incidence of complicated cases was 26.1 per cent in 1935 to 1939, which was approximately the same as that of 25.9 per cent in 1940 to 1944. The interval of time from onset of symptoms to operation was not improved. The higher mortality in advanced age groups is again pointed out. The age distribution was the same for the two periods. The use of drainage was greatly curtailed, without harm to the patient and with a great improvement in the morbidity but probably little effect

on the mortality. The right rectus incision was largely abandoned for the muscle-splitting incision in the right lower quadrant, but this change could not be adequately evaluated. The problems of diagnosis are discussed from the standpoint of the correlation of the pathologist's report with the clinical picture. On the basis of a very rigid standard to confirm the diagnosis of acute appendicitis, it was found that 15 per cent of the patients operated on did not have appendicitis. The other abdominal conditions encountered are listed. Although more accurate diagnosis could greatly improve the results, this was not a factor in the improvement of the mortality. In reviewing the causes of death, it is noted that postoperative generalized peritonitis was almost eliminated as a cause of death during the second five year period. The use of the sulfonamide drugs was given the major share of the credit for this, with the conservative treatment of abscess and peritonitis a contributing factor. To improve results still further, more accurate diagnosis and more effective treatment of the aged are needed.

A third five year report covering the years 1945 to 1949 will be presented to evaluate the addition of penicillin to the treatment of appendicitis.

# TETRAETHYLAMMONIUM CHLORIDE IN EXPERIMENTAL VASCULAR INJURIES OF LIMB, BOWEL AND HEART

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DETROIT

IN THEIR study of quaternary ammonium compounds, Burns and Dale<sup>1</sup> found that tetraethylammonium chloride (TEAC) had a nicotine-like action but was void of either a curare-like or muscarine-like action. The more recent studies of Acheson and Moe<sup>2</sup> showed the action of tetraethylammonium chloride to be one of blockade of the cholinergic ganglions of the sympathetic and parasympathetic nervous systems. After administration of tetraethylammonium chloride the effects of preganglionic stimulation are abolished but not the effects of postganglionic stimulation or of drugs with a peripheral action. According to Loewi,<sup>3</sup> the mechanism of autonomic blockade by tetraethylammonium chloride still remains to be explained.

The generalized autonomic ganglion blockade produced by this drug results in a transient fall in systemic blood pressure and an increase in both peripheral blood flow and skin temperature. These effects, due to the removal of vasoconstrictor tone by action on the sympathetic ganglions, suggested the use of the drug in peripheral vascular disease, such as Raynaud's phenomenon, Buerger's disease, causalgia, reflex dystrophy, thrombophlebitis, trench foot and immersion foot.

One objective of the present study was to determine whether establishment of collateral circulation following experimental injury to a major blood vessel, such as the femoral artery, would be enhanced

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From the Experimental Surgical Laboratory, Harper Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Burns, J. H., and Dale, H. H.: *J. Pharmacol. & Exper. Therap.* **6**:417, 1914-1915.

2. Acheson, G. H., and Moe, G. K.: *J. Pharmacol. & Exper. Therap.* **84**:189, 1945; *ibid.* **87**:220, 1946.

3. Loewi, O.: *J. Pharmacol. & Exper. Therap.* **88**:136, 1946.

by the use of tetraethylammonium chloride. For this purpose we ligated and sectioned the abdominal aorta in dogs and followed the clinical course in both untreated control animals and animals treated with tetraethylammonium chloride. This procedure was thought suitable for our purpose, since Leriche<sup>4</sup> found that the ultimate result of the operation was death from gangrene of the hindlimbs in about seventy-two hours and Mulvihill and Harvey<sup>5</sup> had shown that a generalized reflex vasospasm occurs in collateral vessels when an artery is ligated. Prevention of cyanosis, paralysis and gangrene of the limb and death of the animal could be taken as evidence of the efficacy of tetraethylammonium chloride in preventing reflex vasospasm. While this study was in progress, Cooper, Robertson and Dennis<sup>6</sup> published their results of a similar study with essentially similar findings.

Most of the vascular studies with tetraethylammonium chloride have dealt with the blood supply to the somatic structures, and little is known about its action on the blood vessels supplying the visceral organs. We therefore also undertook some experiments to determine the effects of the drug on the mesenteric and coronary blood vessels. It occurred to us that if the reflex vasospasm usually associated with arterial constriction could be reduced in intestinal and coronary vessels the drug might prove of value in the treatment of mesenteric thrombosis and the anginal syndrome.

#### PROCEDURES

The experiments were carried out on healthy mongrel dogs weighing 15 to 20 pounds (6.8 to 9.1 Kg.). All operations were performed after the animals had been fasted for twenty-four hours; pentobarbital sodium was given intravenously as the anesthetic. Tetraethylammonium chloride<sup>7</sup> was given in nontoxic doses<sup>8</sup> either intramuscularly, 25 mg. per kilogram of body weight, or intravenously, 5 to 6 mg. per kilogram of body weight.

*Ligation of the Abdominal Aorta.*—These experiments were conducted on 29 dogs. The abdominal aorta was ligated just below the inferior mesenteric artery and above the bifurcations. The aorta was then divided between the ligatures, preventing reformation of the continuity of lumen. The circumflex iliac arteries, direct branches from the aorta just below the inferior mesenteric artery, were also ligated, since these form an important source of blood supply to the lower extremity. This origin is in contrast to that in the human being, in whom these vessels are branches of the internal iliac artery.

4. Leriche, R.: *Surgery of Pain*, Baltimore, Williams & Wilkins Company, 1939.

5. Mulvihill, D. A., and Harvey, S. C.: *J. Clin. Investigation* **10**:423, 1931.

6. Cooper, F. W.; Robertson, R. L., and Dennis, E. W.: *Surgery* **22**:740, 1947.

7. The preparation used was etamon,<sup>®</sup> supplied through Dr. E. C. Vonder-Heide, of the laboratory of Parke, Davis & Company, Detroit.

8. Gruhzit, O. M.; Fiskens, R. A., and Cooper, B. J.: *J. Pharmacol. & Exper. Therap.* **92**:103, 1948.

Of the 29 dogs operated on, 14 were used as a control series and were given no tetraethylammonium chloride after operation. The remaining 15 dogs were treated with the drug, starting immediately after ligation of the aorta. These animals were given 25 mg. of tetraethylammonium chloride per kilogram of body weight intramuscularly twice a day, always in the foreleg, because circulation in the hindleg is impaired and absorption is delayed. The drug was continued for three to seven days, with an average of four days. Treatment with the drug was stopped when the dog exhibited no symptoms of weakness or paralysis. No dog was treated for more than seven days.

The presence or absence of collateral vessels was demonstrated in both series of dogs by postmortem arteriograms, with use of a thin solution of barium, acacia and glycerine for injection into the thoracic aorta.

*Studies on the Normal Stomach and Intestine.*—Fluoroscopic and roentgen studies of the stomach and small bowel were made on unanesthetized dogs after administration of barium sulfate by stomach tube. After control observations of gastric peristalsis and gastric emptying of the barium meal, tetraethylammonium chloride was given intravenously in doses of 5 mg. per kilogram and roentgenologic observations continued.

Further studies on the small bowel were made by direct inspection of the exposed organ and by recordings of the serosal temperatures before and after administration of tetraethylammonium chloride, 5 to 6 mg. per kilogram. These studies were made on anesthetized animals, with use of intestinal loops. Serosal temperatures of the small bowel were recorded with a Rauh electrothermocouple. Temperature readings could be instantly made by applying the electrodes to the surface of the bowel. This was a distinct advantage when the response to a drug is as rapid as was the case with tetraethylammonium chloride. Preventing the drying of the serosal surface, controlling room air currents and gentle infrequent handling of the bowel were points which were considered important because any one might distort the normal temperature or normal state of the bowel. When these were standardized, the changes in the temperature readings were considered to result mainly from the drug effect.

Temperature readings were taken from the serosal surface of the small bowel after the loop had been delivered onto the abdominal wall and placed on moist sponges. The loop was treated the same way when normal curves were obtained or when curves after administration of tetraethylammonium were taken.

Twenty dogs were used and many temperature readings taken for both normal and tetraethylammonium chloride curves. In these cases the drug was given rapidly by the intravenous method in a dose of 5 to 6 mg. per kilogram.

*Ligation of Superior Mesenteric Artery.*—After the routine pentobarbital sodium anesthesia, the superior mesenteric artery was isolated and then ligated with heavy silk sutures in 7 dogs. Immediately after the ligation tetraethylammonium chloride was given intramuscularly and continued twice a day, using 25 mg. per kilogram of body weight. These injections were continued until the time of death.

*Ligation of Smaller Mesenteric Vessels (Vasa Recti).*—Sixteen dogs were used in this series of experiments. The vasa recti vessels of various lengths of bowel were ligated with fine sutures. To permit better comparison only the vasa recti in the ileum were used.

Eight pairs of dogs were used; 1 of each pair served as control, while the other was treated with 25 mg. of tetraethylammonium chloride per kilogram



of body weight three times a day. Eight different lengths of bowel, ranging from 3 to 8 cm., were deprived of their blood supply. All measurements were taken on the ileum after ligation and while the bowel was contracted.<sup>9</sup>

*Experimental Strangulation of the Bowel.*—The procedure of Laufman and Method<sup>10</sup> of constricting a segment of small bowel with umbilical tape was used. Segments of small bowel were ligated tightly enough to produce obstruction of venous return but still leave the smaller arcade arteries pulsating. After a period of thirty minutes to one hour the ligatures were released and the serosal temperatures were taken. To check the changes in the segment of bowel injured by the ligature, a normal segment of bowel several feet from the site of obstruction was used as a control. The serosal temperatures were recorded from the normal segment as well as from the portion of bowel previously under the effects of the vascular obstruction. These temperature readings were then repeated after administration of tetraethylammonium chloride.

*Ligation of Coronary Vessels.*—Using a transthoracic approach and positive pressure ventilation via an intratracheal tube, 6 dogs were operated on and the left descending or posterior coronary artery was ligated. Recovery was good, and clinically the animals exhibited no ill effects from the operation. Tetraethylammonium chloride was given intramuscularly, 25 mg. per kilogram twice a day. Electrocardiograms were taken at intervals to determine the effects of the operation and the treatment.

#### RESULTS

*Effects of Tetraethylammonium Chloride Following Ligation of Abdominal Aorta.*—After ligation of the abdominal aorta most of untreated dogs showed the typical paralysis of the hindlegs and evidence of impaired circulation as described by Leriche<sup>4</sup> and Cooper and co-workers.<sup>6</sup> The paralysis was not severe at first but progressed rapidly from coldness and cyanosis to a very evident gangrene of the hindlegs. Within twenty-four to seventy-two hours fatal gangrene developed; 11 of the 14 dogs died of either gangrene or ischemic paralysis. Three control dogs survived the operation but showed a moderate amount of paralysis for three to four days afterward. Thereafter, these 3 animals exhibited claudication in the posterior extremities for four to five weeks. This could be demonstrated by exercising the animals for five minutes. The hindlegs would become completely paralyzed and drag as the animals attempted to walk. However, when the dog was allowed to rest for ten to fifteen minutes, the paralysis disappeared and the strength and ability to walk returned. At the end of five weeks, these 3 animals showed no evidence of impaired circulation on exercise; possibly the collateral circulation was sufficient at this time to prevent these symptoms.

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9. According to F. P. Mall (Johns Hopkins Hosp. Rep. 1:1, 1896), 25 cm. of intestine will shorten to 15 cm. after ligation of the vasa recti. On this basis, the devascularized length of bowel measured in the relaxed condition, would range in our experiments from 5 to about 13 cm.

10. Laufman, H., and Method, H.: Surg., Gynec. & Obst. 85:675, 1947.

In the group of 15 dogs operated on and treated with tetraethylammonium chloride, there was a marked absence of the paralysis, cyanosis and weakness of the posterior extremities so common in the control dogs. A few dogs showed a slight weakness and stiffness, but this was transient and disappeared after a few days of treatment. All but 4 animals of the treated group survived the operation and showed no residual or immediate effects from ligation of the abdominal aorta. They were able to stand and walk normally. No muscular impairment was noted in the hindlegs after exercise. Of the 4 treated dogs which died, in 2 gangrene of the hindlegs developed and 2 died of conditions unrelated to the experiment (distemper and peritonitis). It was observed that when an area of gangrene did develop, further

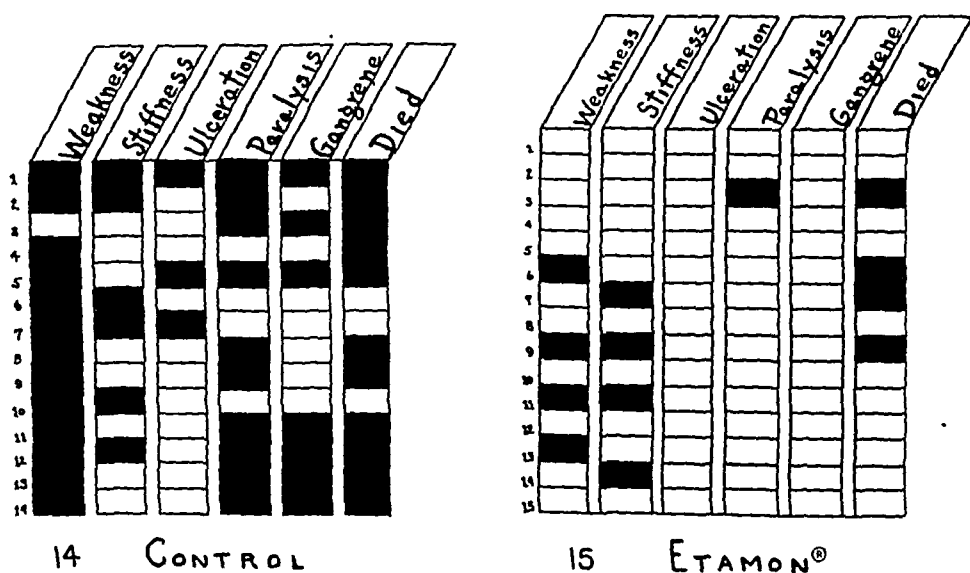


Fig. 1.—Complications in control and etamon®-treated dogs after ligation and division of the abdominal aorta. Each black rectangle indicates the presence of a particular symptom. More complications occurred in the untreated control group.

treatment with tetraethylammonium chloride was of no value in preventing extension of the process.

Figure 1 graphically contrasts the two groups of dogs by comparing the appearance of symptoms in each group. It is easily seen that many more symptoms and fatalities appeared in the control group than in the group treated with tetraethylammonium chloride. In figure 2, *A* and *B*, are arteriograms of control dogs showing the obstruction in the aorta produced at operation and the absence of the radiopaque material in the vessels of the lower extremity. In contrast to this, *C* is an arteriogram of a dog treated with tetraethylammonium chloride, killed five weeks after operation, in which the filling of the vessels of the posterior extremity is good.

*Gross Effects of Tetraethylammonium Chloride on the Normal Stomach and Bowel.*—After administration of 5 to 6 mg. of tetraethylammonium chloride per kilogram intravenously, peristaltic activity of the stomach was abolished. The concomitant gross changes observed in the loop of small bowel exposed on the abdominal wall were more marked and striking. This loop of small bowel became blanched and rippled and appeared to be in spasm. The description of "tiger stripes"

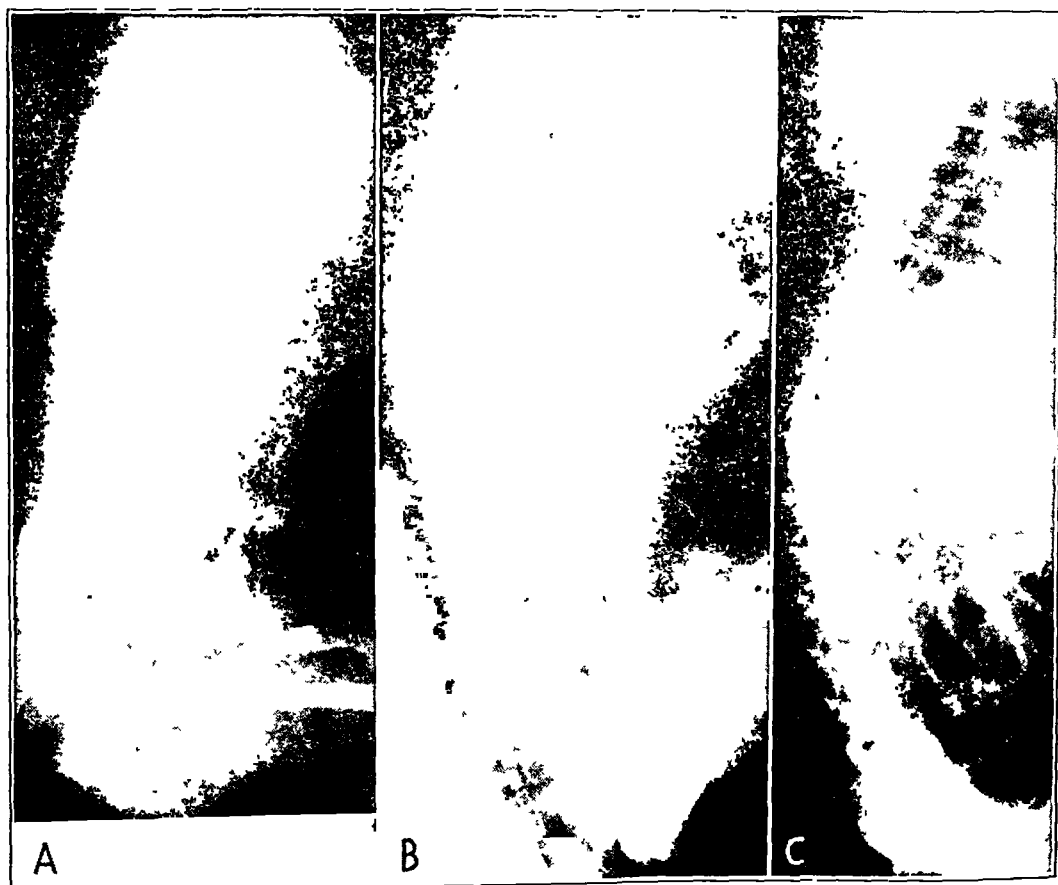


Fig. 2.—*A* and *B*, postmortem arteriograms of control dogs showing the obstruction in the aorta produced at operation and the absence of radiopaque material in the blood vessels of the hindlegs. Both of these animals died of gangrene of the hindlegs. *C*, postmortem arteriogram of an etamon®-treated dog showing the obstruction in the aorta produced at operation, and the abundant blood supply to the lower extremities when contrasted with *A* and *B*. This animal exhibited none of the complications so common in the control series and was killed for the arteriogram.

might fit the appearance of the bowel at this time. These effects lasted fifteen to twenty minutes. Thereafter feeble peristaltic waves began to go through this segment, and the pale appearance of the bowel soon gave way to its normal color.

Roentgenologic studies on unanesthetized dogs confirmed these findings obtained by direct inspection.

*Effect of Tetraethylammonium Chloride on Serosal Temperature of Normal Bowel.*—When the temperatures were recorded for a ten minute period from a loop of normal bowel, a slight fall, usually 1 to 3

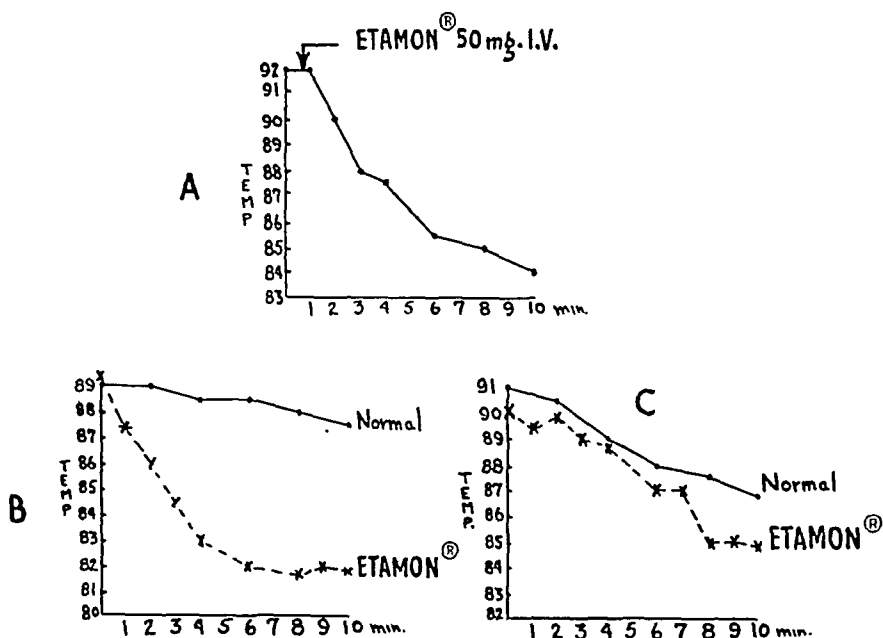


Fig. 3.—A, curve showing the typical rapid fall in the bowel temperature after administering etamon® intravenously and taking serosal temperatures at one minute intervals for ten minutes. B and C, curves showing the contrast between a normal ten minute curve and the same loop after administration of the drug.

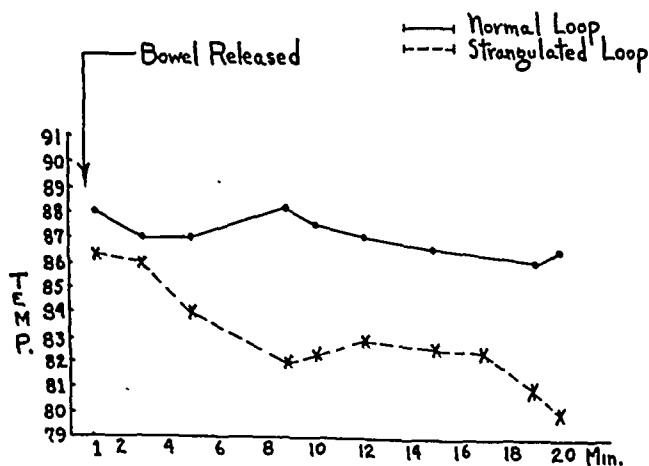


Fig. 4.—Curves showing the temperature responses in a 3 inch loop of normal bowel and a loop of bowel in which the venous return was obstructed for one hour. The fall in serosal temperature was greater in the strangulated loop of bowel.

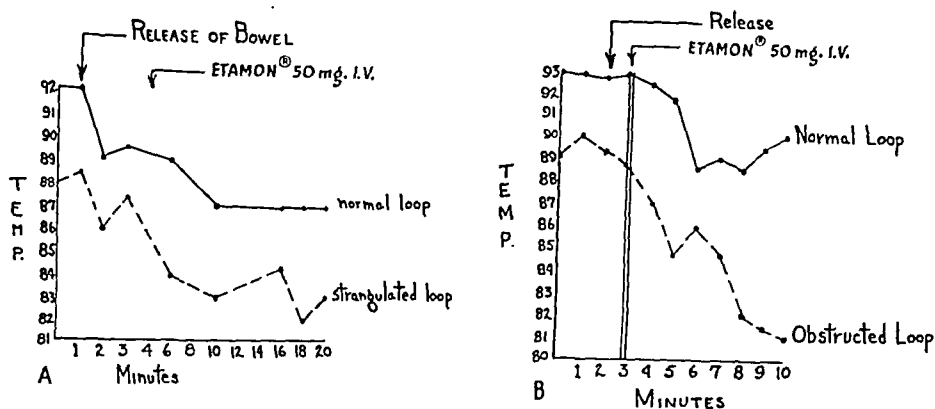


Fig. 5.—Temperature response in bowel after (A) sixty and (B) thirty minutes of venous obstruction and treatment with etamon® intravenously immediately after release of the venous obstruction. Etamon® had no effect as far as altering the serosal temperature was concerned.

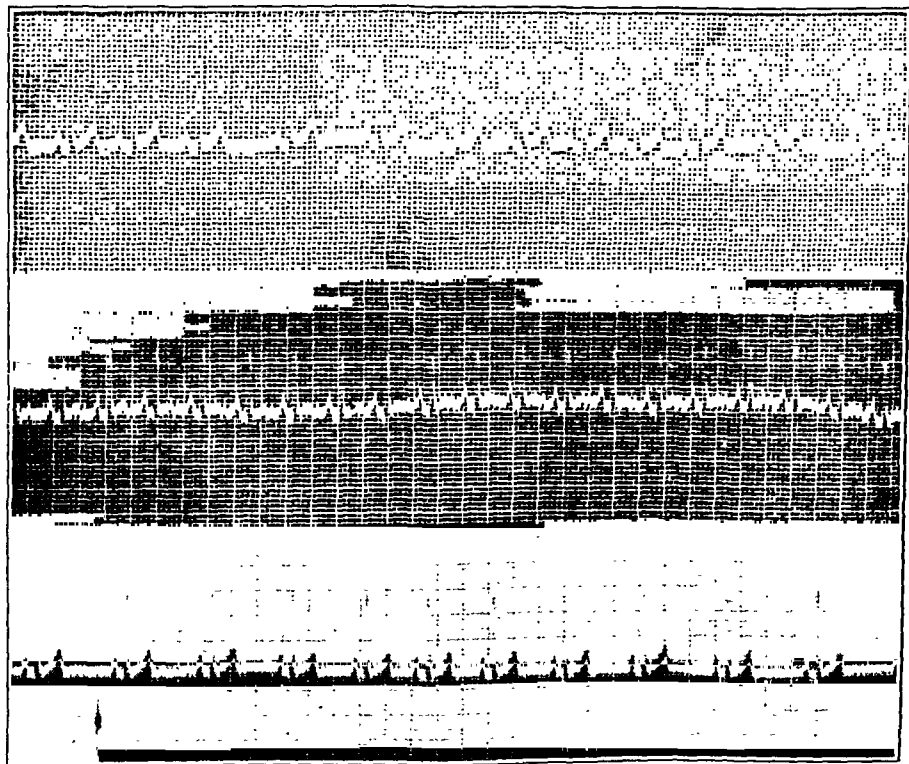


Fig. 6.—Electrocardiogram using normal leads taken on an anesthetized dog showing the effects of the intravenous administration of etamon® on a normal dog heart. The curve appears to be normal for a dog with marked sinus arrhythmia. After administration of etamon®, the rate became very rapid, approximately 155. The P and QRS complexes remained unchanged, but the T waves appeared to become flattened and then inverted. Fifteen minutes later the curve returned to normal.

degrees (F.), was obtained. This could be accounted for by exposure to room air.

When 5 to 6 mg. of tetraethylammonium chloride per kilogram of body weight was given rapidly intravenously, the change was immediate and marked. In every case, there was a marked fall in temperature, averaging 6 degrees. This drop continued for twenty to thirty minutes, reaching its lowest point in about ten minutes. Accompanying this drop in temperature, the appearance of rippling, spasm and blanching was seen in the bowel wall. Curve *A* in figure 3 shows a typical

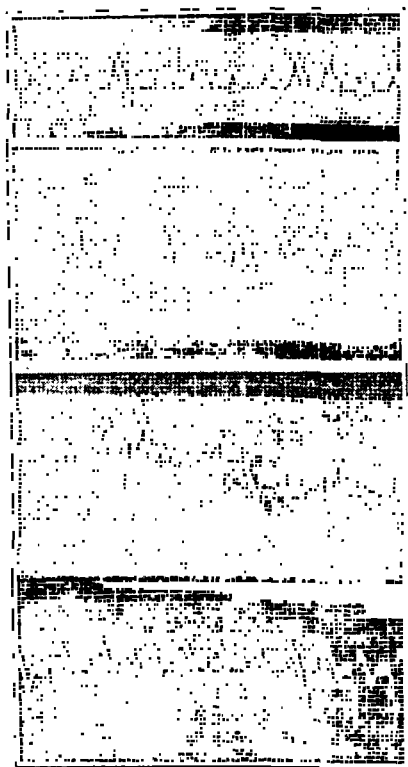


Fig. 7.—The left descending coronary artery was ligated and etamon® given intramuscularly. The electrocardiogram shows no axis deviation. The P-R interval is 0.12 second; the QRS complex, 0.06 second. There are periods of ventricular tachycardia during which P waves are seen acting independently of ventricular beats. The Q wave in lead I is large; the T wave in leads I and II deeply inverted. There are ventricular extrasystoles. The fourth lead shows typical acute coronary occlusion. The S-T segment is elevated, the T wave inverted and the QRS component normal. The diagnosis was acute anterior coronary thrombosis with runs of ventricular tachycardia.

rapid fall in the bowel temperature after administration of tetraethylammonium chloride; curves *B* and *C* show the contrast between a normal ten minute curve and the same loop of bowel after administration of tetraethylammonium chloride.

*Effects of Tetraethylammonium Chloride After Ligation of the Superior Mesenteric Artery.*—All animals died within twenty-four to thirty-six hours after operation and at autopsy showed massive gangrene of the small bowel and cecum. Prior to death these animals showed a bloody diarrhea. Treatment with tetraethylammonium chloride did not prolong the life of the animals, since in untreated animals Scott and Wagensteen<sup>11</sup> found the average survival time of dogs subjected to similar operation to be twenty hours.

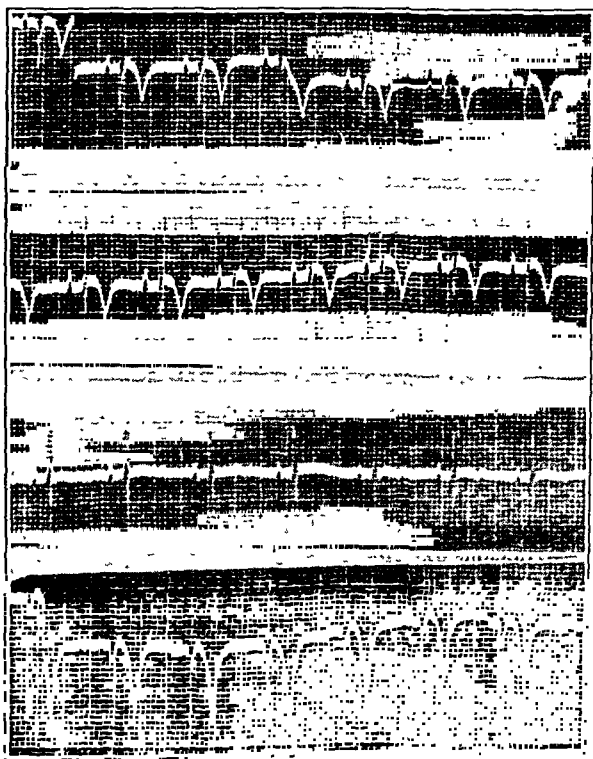


Fig. 8.—This electrocardiogram taken after ligation of the left descending coronary artery and administration of etamon® shows regular sinus rhythm and right axis deviation. The P waves are normal, the P-R interval 0.14 second and the QRS complex 0.05 second. There is no slurring, no R wave in lead I and very minute R waves in leads II and IV. The T wave in leads I and II is exaggerated and inverted, the T wave in lead II huge and inverted. There is some elevation of the segment in leads I, II and IV. There are no further ventricular extrasystoles. The diagnosis was acute anterior massive infarction.

*Effects of Tetraethylammonium Chloride After Ligation of Smaller Mesenteric Vessels.*—The immediate results of ligation of the vasa recti vessels were blanching of the bowel wall, cyanosis and development of areas of spasm. Ultimately the devascularized area became

11. Scott, H. G., and Wagensteen, O. H.: Proc. Soc. Exper. Biol. & Med. 29:424, 1932.

gangrenous. Control dogs survived ligation of the vasa recti only if the bowel area involved was less than 5 cm. in length. When the ischemic area exceeded 5 cm. (measured along the mesenteric border after ligation) the inevitable outcome was gangrene, perforation of this segment and death from peritonitis. The administration of tetraethylammonium chloride did not affect the collateral circulation or the ultimate picture.

*Effects of Tetraethylammonium Chloride After Strangulation of the Bowel.*—In figure 4, the temperature responses of bowel when

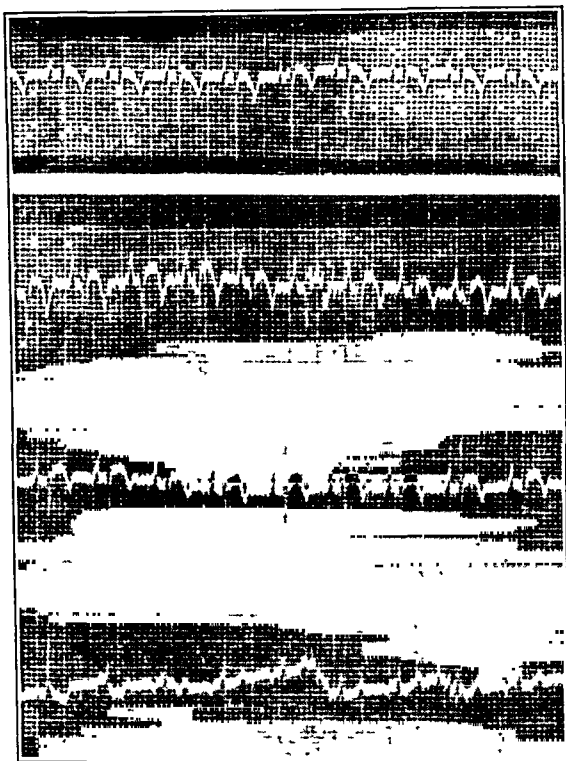


Fig. 9.—The left descending coronary arc was ligated twenty-four hours before the electrocardiogram was taken. The dog was active and its condition appeared good. The electrocardiogram shows regular sinus rhythm with groups of right ventricular extrasystoles in leads II and IV. The P wave is normal, the P-R interval 0.09 second, the QRS complex 0.05 second, without deformity. There is no R wave in leads I and II. The T wave in lead I is sharply inverted, in leads II and III diphasic and in lead IV erect. There is minimal elevation of the S-T segment in lead I and frank elevation and arching in leads II and III. The S-T segment in lead IV is somewhat depressed. The diagnosis was groups of right ventricular extrasystoles and acute posterior infarction.

no treatment was instituted after release of the bowel ligature are seen. It is noted that both the normal and the strangulated loops of bowel showed a fall in the serosal temperature. Figure 5 depicts the results in treated animals after the ligatures were released and



the bowel was relieved of the obstruction. As to dosage, 5 mg. of the drug per kilogram of body weight was used. The fall in temperature of the obstructed loop was greater than that of the control loop in every case, and tetraethylammonium chloride failed to alter the drop in serosal temperatures of either the strangulated or the control loops.

*Effects of Tetraethylammonium Chloride Following Ligation of Coronary Vessels.*—The effect of tetraethylammonium chloride on the electrocardiogram of the normal dog is shown in figure 6. This tracing was obtained by using normal leads. The dose of tetraethyl-

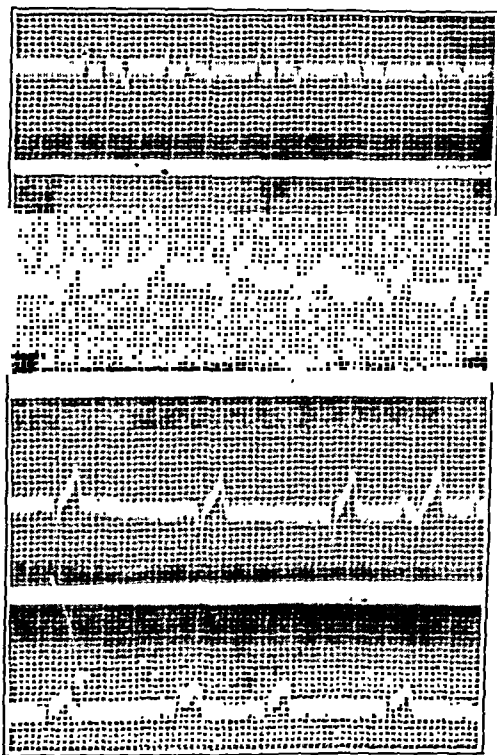


Fig. 10.—The coronary artery was ligated and etamon® given for six days. The dog's condition was very good. The electrocardiogram shows a variable sinus rhythm with stretches of bradycardia, with the auriculoventricular node in control. There are no ventricular extrasystoles. The QRS complex is 0.05 second. The T wave in lead I is small and sharply inverted; elsewhere this wave is erect. The S-T segment in leads II and IV is elevated and is slightly so in lead III. The diagnosis was stretches of bradycardia, with the auriculoventricular node in control, and serious myocardial damage on the basis of coronary blocking but with atypical localization.

ammonium chloride was 50 mg. by vein. The dog showed no ill effects from the drug other than an increase in the heart rate which lasted about fifteen minutes.

Electrocardiograms taken at intervals after coronary ligation revealed no differences between the control group and those treated with tetra-

ethylammonium chloride daily. Figures 7 to 10 are electrocardiographic tracings of animals receiving tetraethylammonium chloride after coronary ligation. When they are compared with figure 6 from a normal dog, it is seen that no outstanding improvement or deterioration can be attributable to the drug.

#### COMMENT

Tetraethylammonium chloride (etamon®) was found to be effective in preventing weakness and gangrene of the hindlegs of dogs after ligation and the division of the abdominal aorta immediately above its bifurcation.

Perhaps this favorable effect is due to the action of the drug on the collaterals which come off cephalad to the site of division of the aorta. These vessels are quite numerous in the dog, especially the internal mammary-epigastric anastomosis in females. The therapeutic effect of the drug, blocking impulses across the ganglions pertaining to these collaterals, causes vascular dilatation.

No favorable effect was observed when the main stem mesenteric vessels were ligated and the drug administered. When the small vessels of the bowel were ligated, administration of the drug produced an unfavorable effect.

The physiologic responses of the autonomic system to the drug are still not completely understood, and the behavior of the drug itself in the hands of different investigators has not been uniform. Different interpretations have been drawn regarding its role in vascular dilatation and the relief of spasm.

DeBakey, Burch, Ray and Ochsner,<sup>12</sup> using careful plethysmograms and recordings of skin temperature of the extremities, found that very little vasodilatation was produced by one intravenous injection of tetraethylammonium chloride.

Pearl,<sup>13</sup> likewise, found that the rise in skin temperature in fingers and toes (the best indication, according to him, of the release of vascular spasm) of patients with peripheral arterial disease was much less after administration of tetraethylammonium chloride than after nerve block with procaine.

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12. DeBakey, M. E.; Burch, G.; Ray, T., and Ochsner, A.: The "Borrowing-Lending" Hemodynamic Phenomenon and Its Therapeutic Application in Peripheral Vascular Disturbances, *Am. J. Surg.* **126**:850, 1947.

13. Pearl, F.: Tetraethyl Ammonium Chloride, Its Effect on Surface Temperatures of Extremities in Peripheral Vascular Conditions, *Am. J. Surg.* **128**:1092, 1948; Effects on Surface Temperatures of Arterio-Sclerotic Extremities, *ibid.* **128**:1100, 1948.

Brown, Allen and McCraig<sup>14</sup> found that the drug would reduce blood pressure of hypertensive patients much more readily after sympathectomy than before the operation. One half to one third the amount was effective after sympathectomy, and the effect lasted longer. The group of patients were of the type in whom sympathectomy does not readily reduce blood pressure to normal, but 200 mg. of the drug produced this effect in most of them. These authors expressed the belief that the drug does not act in a more concentrated manner on the ganglions which remain after sympathectomy, because very large doses before sympathectomy did not reduce the blood pressure of hypertensive patients to normal. They felt, rather, that in some way either the arterioles became more susceptible to the drug or that the remaining ganglions might be more completely blocked after operation than before.

Laufman,<sup>15</sup> by direct microscopy on the small arterioles of the dog, has emphasized the tremendous role which reflex spasm plays when an artery or vein is occluded. Temporarily occluding the mesenteric vein will cause the small arteries to contract to one eighth their normal size, and this residual spasm will remain for a considerable time. He has given the following explanation of our failure to observe any benefit from the drug after mesenteric ligation<sup>16</sup>: Strangulation of a loop of bowel is analogous to a peripheral vascular occlusion. There is stimulation of the afferent sympathetic nerve fibers and ganglions, with resulting reflex vasospasm of the segment of bowel involved. Occlusion and division of a small mesenteric vessel or even handling the mesentery of the bowel produces a similar spasm. When the drug is given to such an animal it apparently dissipates itself by acting on the unstimulated ganglions in the rest of the body, since these are the paths of least resistance. The ganglions harboring the stimulus of the occlusion are thereby left relatively unaffected by the action of the drug. This is especially true if the stimulus is strong. Consequently, the general vasodilatation in other parts of the body results in the removal of blood from the stimulated area. Thus additional local spasm is produced rather than dilatation, and thus a reversal of the effect from the drug is caused.

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14. Brown, H. S.; Allen, E. V., and McCraig, W.: The Effect of Tetraethyl-Ammonium Chloride on Blood Pressure Before and After Sympathectomy for Hypertension, *Proc. Staff Meet., Mayo Clin.* **23**:94, 1948.

15. Laufman, H.; Martin, W. B., and Tuell, S. W.: Rationale of Therapy in Acute Vascular Occlusions Based on Micrometric Observations, *Ann. Surg.*, to be published.

16. Laufman, H.: Personal communications to the authors.

## CONCLUSIONS

1. Experimentally, tetraethylammonium chloride (etamon®) is of definite value in preventing ischemic gangrene, muscular weakness and subsequent paralysis produced when the aorta is ligated and divided just above the bifurcation. The use of this drug in certain injuries of peripheral vessels appears to be of value.

2. The action of tetraethylammonium chloride observed on the mesenteric vessels does not appear to be analogous to the action observed in peripheral vessels.

3. Vasospasm is not prevented or abolished by tetraethylammonium chloride when it occurs in the mesenteric vessels or in the intestinal musculature. Further evidence of the inability of the drug to relieve vasospasm is noted by the fall in serosal temperature.

4. Tetraethylammonium chloride is not indicated in mesenteric thrombosis or in mechanical intestinal obstruction as an agent for the relief of vasospasm occurring in these conditions. Likewise, the drug is not advocated as a means of determining the viability of a previously strangulated loop of bowel in which vascular occlusion has occurred.

5. Neither detrimental nor advantageous effects were observed in dogs after experimental ligation of coronary vessels.

## EFFECT OF DISTENTION ON INTESTINAL REVASCULARIZATION

RUDOLF J. NOER, M.D.

AND

JOHN WILLIAM DERR, M.D.

DETROIT

**D**ISTENTION of the small intestine has been shown to exert a deleterious effect on the blood flow through the intestinal wall in experimental animals and it is reasonable to expect some degree of correlation between the findings in animals and the situation in man. Indirect evidence that this is true is to be found in gross and microscopic study of material observed in the operating room and at autopsy. Direct observation, however, of the precise effect of varying degrees of distention on the intramural circulation in man during life presents obvious difficulties. It therefore seems worth while to present data based on the use of injection technics in the study of human autopsy material.

Intraluminal pressures in obstructed intestines of dogs have been measured by Owings, McIntosh, Stone and Weinberg<sup>1</sup>; Burget, Martzloff, Suckow and Thornton<sup>2</sup>; Antoncic and Lawson<sup>3</sup>; Sperling, Paine and Wangenstein,<sup>4</sup> and others. These studies were carried out in the living animal intestine. The results are therefore not directly applicable to the present study of excised human intestine, which obviously con-

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This investigation was supported by a research grant from the Division of Research Grants and Fellowships of the National Institute of Health, U. S. Public Health Service.

1. Owings, J. C.; McIntosh, C. A.; Stone, H. B., and Weinberg, J. A.: Intraintestinal Pressure in Obstruction, *Arch. Surg.* **17**:507 (Sept.) 1928.

2. Burget, G. E.; Martzloff, K.; Suckow, G., and Thornton, R. C. B.: The Closed Intestinal Loop: I. Relation of Intraloop (*Jejunum*) Pressure to the Clinical Condition of the Animal, *Arch. Surg.* **21**:829 (Nov.) 1930.

3. Antoncic, R. F., and Lawson, H.: The Muscular Activity of the Small Intestine in the Dog During Acute Obstruction, *Ann. Surg.* **114**:415, 1941.

4. Sperling, L.; Paine, J. R., and Wangenstein, O. H.: Intra-Enteric Pressure in Experimental and Clinical Intestinal Obstruction, *Proc. Soc. Exper. Biol. & Med.* **32**:1504, 1935.

siders only the purely mechanical effect of distention on the intramural vessels. Sperling, Paine and Wangenstein<sup>4</sup> also measured the intraenteric pressure in 5 cases of mechanical obstruction of the small bowel at the time of enterostomy by connecting the enterostomy tube to a manometer. Sustained pressures varied between 4 and 18 cm. of water, whereas pressures of 20 to 30 cm. developed during active peristalsis. Reports of accurate determination of intraluminal pressures in distended human intestine in the unopened abdomen without concomitant decompression have not been found. This is obviously a difficult problem but one deserving of further investigations.

Van Zwalenburg<sup>5</sup> (1907) inserted a cannula, carrying a small lamp, into the lumen of the intestine of the dog and studied the effect of intraenteric pressures on the blood flow through the intestinal wall by means of low power microscopy. His report is as follows:

At 30 mm. mercury pressure we found that some capillary streams were arrested. At 60 mm. many small veins had their currents arrested, and in most of them the stream was so slow that individual corpuscles could be seen. At 90 mm. all blood streams were moving slowly and many were not moving at all. One was impressed with the difficulties encountered by the circulation in its attempt to find some point of least resistance through which the stream might insinuate itself. Currents would at one time go in one direction and the next moment in the opposite. At the point of branching of vessels, streams were seen going in all sorts of directions.

At 130 mm. all circulation had ceased—the corpuscles standing still in the blood vessels. Many vessels, however, still carried the impulse of the heart beat—the corpuscles moving to and fro, but retaining their relative positions in the field. This pulsation was seen in some of the largest and the most superficial arteries after the pressure was carried up to 250 mm.

Gatch, Trusler and Ayres<sup>6</sup> (1927) studied blood flow through the intestinal wall in dogs by collecting all venous return from isolated obstructed loops. The rate of return flow was inversely proportional to the degree of distention. They also noted a constant residual blood flow from anastomotic vessels in the mesentery and along the mesenteric border, however great the distention. Complete anemia was observed on the antemesenteric border of the bowel when the intraenteric pressure equaled the systemic blood pressure. Morton<sup>7</sup> (1929) presented low power photomicrographs of injected duodenum and ileum of the dog with and without distention. The interference with filling of the

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5. Van Zwalenburg, C.: Strangulation Resulting from Distention of Hollow Viscera, *Ann. Surg.* **46**:780, 1907.

6. Gatch, W. D.; Trusler, H. M., and Ayres, K. D.: Effects of Gaseous Distention on Obstructed Bowel, *Arch. Surg.* **14**:1215 (June) 1927.

7. Morton, J. J.: Differences Between High and Low Intestinal Obstruction in the Dog: Anatomic and Physiologic Explanation, *Arch. Surg.* **18**:1119 (April) 1929.

finer vessels produced by distention is well shown, although the degree of intraenteric pressure is not stated. Dragstedt, Lang and Millet<sup>8</sup> (1929) reported effects of intraenteric pressures on venous return from the duodenum, jejunum, ileum and colon of the dog and amplified their findings by observations of the transilluminated intestinal wall. Interruption of venous flow occurred at pressures of 35 to 40 mm. of mercury in the jejunum and 55 to 60 mm. in the ileum. Their studies indicated that this obstruction occurred in the wall of the intestine and not in the mesentery. They confirmed the findings of Gatch and his associates<sup>9</sup> as to the residual flow from the mesenteric veins which no amount of intraenteric pressure would abolish. Herrin and Meek<sup>9</sup> reported in 1933 that intraluminal pressures of 50 to 80 mm. of mercury in the dog reproduced the entire clinical picture of intestinal obstruction even though patency of the intestinal lumen was maintained. Gatch and Culbertson<sup>10</sup> (1935) reported that pressures as low as 20 mm. of mercury may produce almost complete ischemia of the intestinal mucosa of the dog. Sperling and Wangenstein<sup>11</sup> (1935) were able to prevent absorption of strychnine from closed ileal loops by intraluminal pressures greater than 100 mm. of mercury and could elicit a strychnine effect only after reduction of pressures below 70 mm. Absorption occurred more readily after damage of the intestinal wall by protracted distention.

Lawson and Chumley<sup>12</sup> (1940) studied differential pressures between systemic vessels and those supplying isolated loops of ileum in dogs. Blood flow was only momentarily interrupted by pressures below 30 mm. of mercury. Higher pressures below mean arterial pressure produced marked initial reduction in flow, followed by partial recovery in a few seconds. Denervation did not alter the results, and they suggest intrinsic nervous mechanisms as the means for compensation. Oppenheimer and Mann<sup>13</sup> (1943), transilluminating the wall of the

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8. Dragstedt, C. A.; Lang, J. F., and Millet, R. F.: The Relative Effects of Distention on Different Portions of the Intestine, *Arch. Surg.* **18**:2257 (June) 1929.

9. Herrin, R. C., and Meek, W. J.: Distention as a Factor in Intestinal Obstruction, *Arch. Int. Med.* **51**:152 (Jan.) 1933.

10. Gatch, W. D., and Culbertson, C. G.: Circulatory Disturbances Caused by Intestinal Obstruction, *Ann. Surg.* **102**:619, 1935.

11. Sperling, L. and Wangenstein, O. H.: Transperitoneal Absorption: VI. Significance of Impaired Viability and Influence of Distention on its Occurrence, *Proc. Soc. Exper. Biol. & Med.* **32**:1385, 1935.

12. Lawson, H., and Chumley, J.: The Effect of Distention on Blood Flow through the Intestine, *Am. J. Physiol.* **131**:368, 1940.

13. Oppenheimer, M. J., and Mann, F. C.: Intestinal Capillary Circulation During Distention, *Surgery* **13**:548, 1943.

rat intestine, found no change in the intraparietal capillary circulation at pressures of 10 to 20 mm. of mercury. At 30 to 50 mm. there was increasing interference with capillary circulation, while at 60 mm. "all capillary flow had ceased and only in the largest vessels was blood flowing rapidly. At 70 mm. no flow was seen except in one or two large vessels (arterioles and venules) which had a sluggish, oscillating flow and at 80 mm. even this had stopped."

As stated earlier, direct observation of blood flow through the wall of the living human intestine is difficult to observe, and to our knowledge no correlation of such observations with the degree of intraenteric pressure has been reported. Van Beuren<sup>14</sup> (1929) presented an interesting account of the effect of distention on the vessels of the intestinal wall. His illustrations, concerned chiefly with intestinal perforations following distention, include photomicrographs of dog intestine and human autopsy material. Pressure measurements are not included, but the circulatory effects presumably produced by distention are well demonstrated.

Experimental data from these laboratories<sup>15</sup> indicate that injection studies of excised intestine can be utilized for guarded inferences as to the situation existing in life. Investigation of routes for revascularization following experimental mesenteric occlusion indicated that the maximum degree of devascularization compatible with life of the experimental animal was likewise the maximum area which could be filled through collateral channels by injection technics. Circulatory interruption of sufficient extent to cause death of the animal also resulted in failure to fill similar areas by injection. It thus appears that injection technics may be utilized for investigation of circulatory situations in man which cannot otherwise be attacked with presently available methods.

#### METHODS

Human autopsy material was utilized for all these studies, the entire small intestine being removed as soon after death as possible, with the blood supply preserved intact. Twenty such specimens, varying between 18 and 20 hours post mortem, were used. Good injections were obtained in all cases, although capillary filling was invariably more nearly complete in the fresher material. Extravasations occurred but rarely and only in the longer dead intestines. Loops chosen for study were all from the lower part of the jejunum or the upper part of the ileum. In every case the entire intestine was injected through the superior mesenteric artery, thus providing normal areas for comparison with the degree of filling obtained in the distended loops.

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14. Van Beuren, F. T. Jr.: The Mechanism of Intestinal Perforation Due to Distention, *Ann. Surg.* **83**:69, 1926.

15. Derr, J. W., and Noer, R. J.: Experimental Mesenteric Vascular Occlusion, *Surg., Gynec. & Obst.*, to be published. Noer, R. J., and Derr, J. W.: Revascularization Following Experimental Mesenteric Vascular Occlusion, *Arch. Surg.* **58**:576 (May) 1949.



India ink diluted in bovine plasma proved the best medium. There is little diffusion of this material, and viscosity determinations indicate that it closely approximates the viscosity of blood. All injections were made at room temperature, at pressures between 100 and 150 mm of mercury. Slightly more rapid filling was obtained with the higher pressures, but complete filling was routinely obtained with pressures of 100 mm of mercury or even lower. Drying of the intestine was avoided by repeated spraying of the surface with an atomizer.

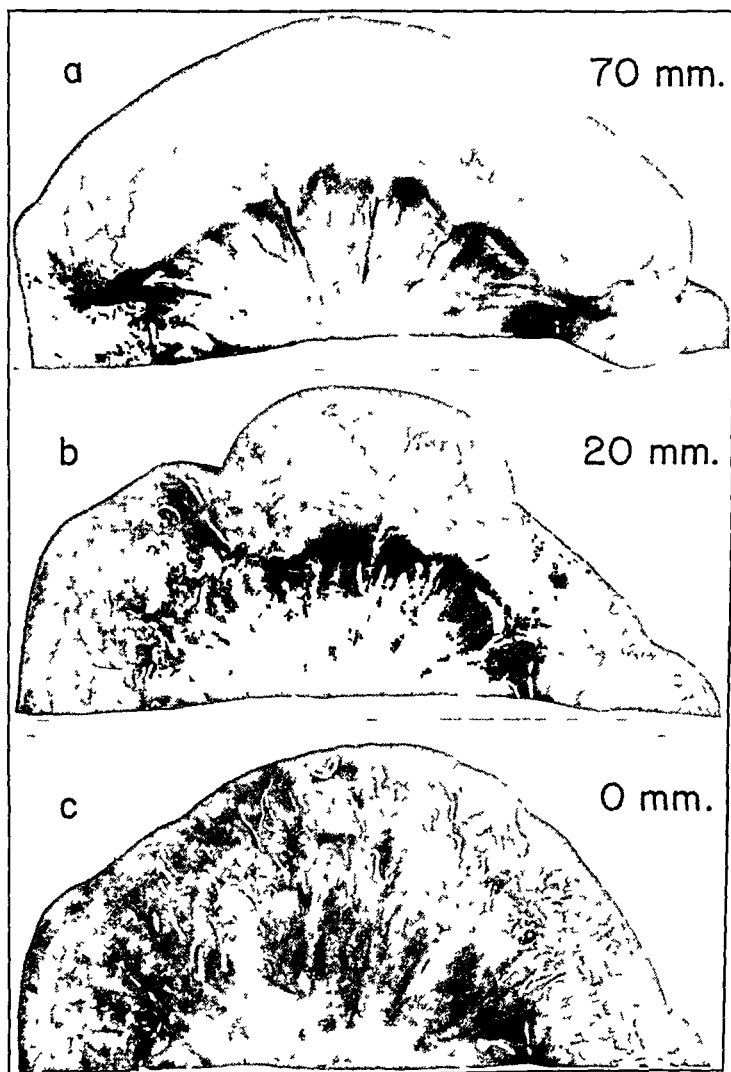


Fig. 1—Specimens of human intestine injected with india ink after distention. Note absence of filling at pressure of 70 mm. of mercury and filling of the larger arteries at 20 mm but complete filling only after release of distention. Unfortunately, the contrast between filled and noninjected intestine, seen clearly in color cinephotography, is not adequately reproduced in black and white.

Intraenteric distention was produced by air inflation of a condom balloon introduced into the loop being studied, the pressure measured by a mercury manometer. This may introduce an error in pressure measurement equal to the inherent resistance of the latex balloon. Inflation of this balloon to the size

ordinarily used in the course of the experiments was found to require pressure of not more than 5 mm. of mercury. Actual intraenteric pressures in these experiments may therefore be approximately 5 mm. of mercury less than the recorded pressures which are reported. Injections were started above 70 mm. of mercury (this being the pressure required to prevent filling in most instances), and injecting pressure was constantly maintained throughout the process of gradual deflation of the balloon by steps of 10 mm. each.

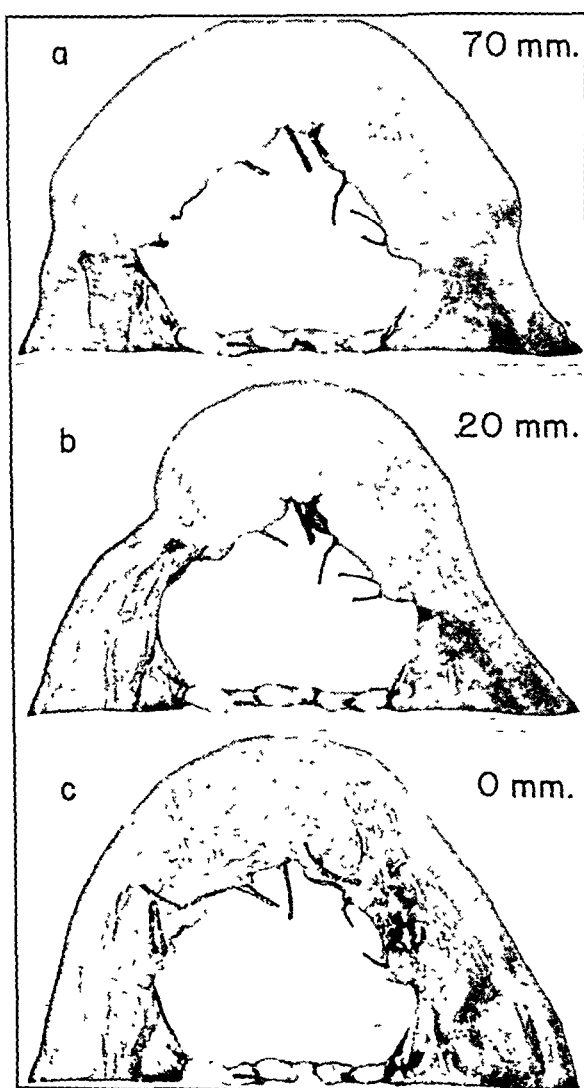


Fig. 2.—Specimens of human intestine injected with india ink after division of the vasa recta followed by distention. Note that no filling of the loop occurs while distention remains but that good vascular filling is obtained after deflation (compare with figure 1).

Results were recorded for repeated study by slow motion cinephotography (films taken at 32 frames per second were projected for study at 16 frames per second, thus reducing the apparent speed of injection by approximately one half).

Some of the specimens were preserved by fixation in formaldehyde solution U.S.P. and cleared by a previously described modification of the Spalteholz technic.<sup>16</sup>

### RESULTS

Intraenteric pressures of 70 mm. of mercury or higher prevent filling of the distended area of the intestine, even when all the mesenteric vessels remain intact. Gradual deflation reveals that the larger arteries begin to fill at 60 to 50 mm., and that they are fairly well injected at pressures of 20 to 30 mm. Complete capillary filling, however, does not occur until complete deflation has been produced (fig. 1).

Ligation of the vasa recta supplying the distended loop greatly accentuates the interference with filling produced by distention, since all filling must then take place by means of anastomoses within the intestinal wall. In these circumstances the distended loop fills only from its extremities as the balloon is deflating in these areas; the central portion of the loop remains uninjected until complete deflation of the balloon has been accomplished (fig. 2).

### COMMENT

It should be recognized at the outset that the situation which exists in the excised, nonviable intestine is vastly different from that which exists in life. Such factors as vasodilation and vasoconstriction, contractility of muscle and variations in tissue tension must all be of great importance in determining the reaction of the intestine and its circulation to varying degrees of distention. However, these very factors tend to complicate the entire picture and make interpretation of their individual importance a matter of considerable difficulty.

The studies here reported represent a simple and direct approach to the purely mechanical effect of distention on the vessels lying within the wall of the intestine. The results, for the most part, are in accord with opinions expressed by many investigators, and they differ but little from what might be predicted on the basis of various animal experiments. However, it appeared worth while to present the findings for reemphasis of the fact that distention, even in minor degrees, results in definite and often serious interference with the circulation within the intestinal wall. Whether the various physiologic factors mentioned increase or decrease this circulatory embarrassment, we are not prepared to say. Certain it is, however, that the purely mechanical effect of distention as herein demonstrated presents a serious hazard to the patient with intestinal distention, whatever the cause. The urgent need for prompt and complete decompression of the intestine is obvious.

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16. Noer, R. J.: The Blood Vessels of the Jejunum and Ileum: A Comparative Study of Man and Certain Laboratory Animals, *Am. J. Anat.* **73**:293, 1943. Lathrop, G. E., and Krupp, R.: Microscopy of Latex Rubber-Injected Specimens, *Am. J. Clin. Path.* **14**:128, 1944.

## CONCLUSIONS

Injection studies of the effect of distention on the intramural vessels of excised human small intestine reveal the following facts:

1. Intraenteric pressures above 70 mm. of mercury prevent filling of all vessels within the wall.
2. When the vasa recta and arcuate vessels remain intact, the larger arteries will fill despite intraluminal pressures of 20 to 40 mm. of mercury.
3. Complete capillary filling can be obtained only when the intraenteric pressure is less than 10 mm. of mercury.
4. Interruption of the vasa recta supplying a distended loop results in inability completely to inject this partially devascularized loop until distention has been eliminated.

## OBSERVATIONS IN STRANGULATION OBSTRUCTION

### II. The Fate of Sterile Devascularized Intestine in the Peritoneal Cavity

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HAROLD METHOD, M.D.

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AND

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CHICAGO

IN EACH of the several extensive reviews on the subject of intestinal strangulation obstruction,<sup>1</sup> certain questions concerning the nature of toxicity have been left open for speculation. With the advent of such therapeutic advances as replacement of fluids and electrolytes, broader use of blood transfusion, antibiotic therapy and intubation, great strides have been made toward lowering the basic mortality as well as the operative mortality. These advances, great as they are in the therapeutic sense, served in recent years to cool experimental interest in the nature of the toxicity in this affliction. However, during World War II much work was done along parallel lines on the general problem of tissue autolysis in shock, and a large part of the work is directly applicable to the problem of strangulation. Chemotherapy and antibiotic therapy have opened new avenues both in experimental investigation and in clinical practice, since the control of the bacterial factor of the toxicity has resulted in a remarkable diminution of the ill effects from loop strangulations.

The extensive experimental background is well known to those interested in the pathologic physiology of intestinal obstruction, but

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Aided by a grant from the Lois C. Grunow Surgical Fund.

From the Departments of Surgery and Bacteriology, Northwestern University Medical School.

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1. (a) Aird, I.: Morbid Influences in Intestinal Obstruction and Strangulation, *Ann. Surg.* **114**:385, 1941. (b) Besser, E. L.: Cause of Death in Cases of Mechanical Intestinal Obstruction, *Arch. Surg.* **41**:970 (Oct.) 1940. (c) Cooper, H. S. F.: The Cause of Death in High Obstruction in Dog: Anatomic and Physiologic Explanation, *ibid.* **17**:919 (Dec.) 1928. (d) Morton, J. J.: Differences Between High and Low Intestinal Obstruction, *ibid.* **18**:1119 (April) 1929.

it might be advisable to review briefly a few of the crucial experiments in this field.

It has been known for many years from the work of Stone, Bernheim and Whipple<sup>2</sup> that neither frank septicemia nor the loss of fluids and electrolytes from vomiting could explain death from intestinal obstruction. Since these investigators introduced the technic of the isolated loop experiment, which did away with the factor of obstruction, much work has been done by the use of this technic to demonstrate the effects of strangulation. Davis and Stone<sup>3</sup> and Murphy and Brooks<sup>4</sup> were among the investigators who believed that toxins arose from such a loop. Dragstedt,<sup>5</sup> in similar experiments, washed the loops out with ether and found that this diminished the toxicity.

Strangulation experiments of many types have been performed. It has been shown repeatedly that if a loop of intestine of medium length is strangulated within a sterile bag to prevent peritoneal absorption, death is delayed indefinitely provided the lumen is reconstituted. In the absence of the bag, death occurs within two to five days, not necessarily from peritonitis and without septicemia.<sup>6</sup>

Much subsequent work was devoted to the question of the similarity of the toxic picture in strangulation to that of shock. Indeed, fresh postmortem studies showed "wet" organs, indicating a generalized state of increased capillary permeability.<sup>7</sup> Many searches have been made for substances which might produce this state. Among some of the substances which have been implicated are histamine,<sup>8</sup> H substance,<sup>8</sup> adenosine triphosphate<sup>9</sup> and leukotaxine,<sup>10</sup> as well as others. That one

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2. Stone, H. B.: Bernheim, B. M., and Whipple, G. H.: Intestinal Obstruction: A Study of the Toxic Factors, *Bull. Johns Hopkins Hosp.* **23**:159, 1912.

3. Davis, D. M., and Stone, H. B.: Studies on the Development of Toxicity in Intestinal Secretion, *J. Exper. Med.* **26**:687, 1917.

4. Murphy, F. T., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Causes of Symptoms and Death, *Arch. Int. Med.* **15**:392 (March) 1915.

5. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Intestinal Obstruction: II. A Study of the Factors Involved in the Production and Absorption of Toxic Materials from the Intestine, *J. Exper. Med.* **30**:109, 1919.

6. Aird, I., and Henderson, W. K.: Intestinal Strangulation: The Histamine Content of the Peritoneal Transudate from Strangulated Intestinal Loops, *Brit. J. Surg.* **24**:777 (April) 1937.

7. Moon, V. H.: Shock and Related Capillary Phenomena, New York, Oxford University Press, 1938.

8. Dale, H. H.: Conditions Which are Conducive to Production of Shock by Histamine, *Brit. J. Exper. Path.* **1**:103, 1920.

9. Bielschowsky, M., and Green, H. M.: Shock Producing Factor(s) from Striated Muscle: II. Fractionation, Chemical Properties and Effective Doses. *Lancet* **3**:153, 1943.

or all of these substances are produced and absorbed by way of the peritoneal surface cannot be denied; yet their mode of production has not been altogether clarified. A further complication in the assumption that these substances are toxic is the fact that subsequent injections of these substances into healthy animals do not always produce the physiologic state seen in the animal with a strangulated loop, even when the factor of obstruction is accounted for. It is possible, therefore, that these substances are merely a reflection of the primary morbid changes, rather than the cause of the toxicity itself.

In the first article of the present series, Laufman and Freed<sup>10</sup> demonstrated the presence of a substance resembling leukotaxine in the transudate from strangulated loops. This substance invariably produced increased capillary permeability and could be neutralized to a certain degree by adrenal cortex extract. The substance was less potent when filtered free of bacteria but still gave a positive reaction to the Menkin test<sup>11</sup> for the production of increased capillary permeability. This led to an attractive theory that, since local fluid loss from the involved loop was insufficient to account for death, a leukotaxine-like substance might produce a state of local and generalized increased capillary permeability and even a state of shock and might account for the tremendous loss of fluid accompanying strangulation obstruction<sup>12</sup> as well as the "wet" organs<sup>7</sup> usually found post mortem. The concomitant work of Abraham and associates at Oxford<sup>13</sup> tended to support this theory. These workers found that large doses of sterile peptic digests contain permeability-increasing polypeptides which, however, only occasionally caused death, although hemocentration was usually present. Autolytic products alone, while producing local loss of fluid in the peritoneal cavity, did not usually produce general effects after absorption which led to a shocklike state. The investigators concluded, however, that the presence of large masses of autolyzing tissue, such as muscle, must liberate substances of a polypeptide nature which affect profoundly the local blood vessels, causing increased capillary permeability and hence the escape of plasma, thus contributing to the state of shock.

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10. Laufman, H., and Freed, S. C.: Observations in Intestinal Strangulation: I. The Effect of Adrenal Cortical Extract on Its Toxicity, *Surg. Gynec. & Obst.* **77**:605, 1943.

11. Menkin, V.: Effect of Leukotaxine on Cellular Permeability and on Cleavage Development, *Proc. Soc. Exper. Biol. & Med.* **44**:588, 1940.

12. Fine, J.; Fuchs, F., and Gendel, S.: Changes in Plasma Volume Due to Decompression of Distended Small Intestine, *Arch. Surg.* **40**:710 (April) 1940.

13. Abraham, E. P.; Brown, G. M.; Chain, E.; Florey, H. W.; Gardner, A. D., and Sanders, A. G.: Tissue Autolysis and Shock, *Quart. J. Exper. Physiol.* **30**:79 1940; **31**:41, 1942.

For our present purpose, the question arose as to whether autolysis of devascularized intestinal tissue contributes to the state of toxicity over and above the contribution by the bacteria. The present report deals with the effects of autolysis of intestinal tissue in the peritoneal cavity in the relative absence of bacteria.

Various types of dead tissue have been placed into the peritoneal cavities of experimental animals by other investigators. Andrews and associates<sup>14</sup> placed a detached piece of liver in the free peritoneal cavity and found it to cause death. Ellis and Dragstedt<sup>15</sup> did liver implantation experiments and regarded the lethal outcome the result of bacterial toxemia rather than toxemia due to absorption of autolytic products. They indicated that organisms are apparently normal saprophytes of tissue and hence most workers had been quite unable to obtain adult tissues free from bacteria. When they implanted fetal livers obtained by cesarean section, eventual absorption took place without evidence of toxicity.

Mason and Richardson,<sup>15a</sup> using blood pressure as an index of shock following the intravenous injection of filtrates of peripheral muscle, have shown that when the action of bacteria was prevented during autolysis the injection of the resulting filtrates produced no appreciable effect. When bacteria were allowed to grow during autolysis, the filtrate caused a marked drop in blood pressure followed by a rise. Green and Bielschowsky<sup>16</sup> planted striated leg muscle into the peritoneal cavities of animals without antibacterial protection. The toxic effects thus produced were assumed to stem from proteolysis alone. Chemical analysis indicated that adenosine triphosphate was the responsible agent. It has been shown that less than 5 Gm. per kilogram of wet muscle tissue causes no ill effect but more than this amount causes toxicity and death when placed in the peritoneal cavity. This was true whether the muscle was extracted and powdered<sup>17</sup> or used in its fresh state. These experiments, too, were done before the advent of antibiotic drugs. Yet Parsons and Phemister in 1930<sup>18</sup> implanted the

14. Andrews, E.; Rewbridge, A. G., and Hrdina, L.: Causation of *Bacillus Welchii* Infections in Dogs by Injection of Sterile Liver Extracts, *Surg., Gynec. & Obst.* **53**:176, 1931.

15. Ellis, J. C., and Dragstedt, L. R.: Liver Autolysis in Vivo, *Arch. Surg.* **20**:8 (Jan.) 1930.

15a. Mason, E. C., and Richardson, D. L.: Traumatized Muscle Tissue as a Factor in the Production of Shock, *Surg., Gynec. & Obst.* **85**:71, 1947.

16. Green, H. N.: Shock-Producing Factor(s) from Striated Muscle: I. Isolation and Biological Properties, *Lancet* **2**:147, 1943. Bielschowsky and Green.<sup>9</sup>

17. Muirhead, E. E., and Hill, J. M.: Shock Resulting from the Implantation Intraperitoneally of Reconstituted Desiccated Muscle, *J. Lab. & Clin. Med.* **29**:337, 1944.

18. Parsons, E., and Phemister, D. B.: Hemorrhage and "Shock" in Traumatized Limbs: Experimental Study, *Surg., Gynec. & Obst.* **51**:196, 1930.



rectus abdominis muscle into the peritoneal cavities of 2 dogs without producing toxic symptoms. Laufman and Method<sup>19</sup> recently implanted 6 Gm. per kilogram of leg muscle into the peritoneal cavities of dogs protected with adequate doses of penicillin. The animals showed no ill effects, and several weeks later almost no trace of the previously implanted muscle could be found. Aird<sup>18</sup> placed strips of embryo guinea pig intestine into the peritoneal cavities of cats. Such strips were sterile and caused no deleterious effects, dissolving after several weeks. When bacteria were introduced together with the embryo intestine, the host animals died.

This brief perusal of the pertinent literature indicates that sterile tissue placed in the peritoneal cavity will undergo autolysis without producing either a shocklike state or death. If this is so, we thought that

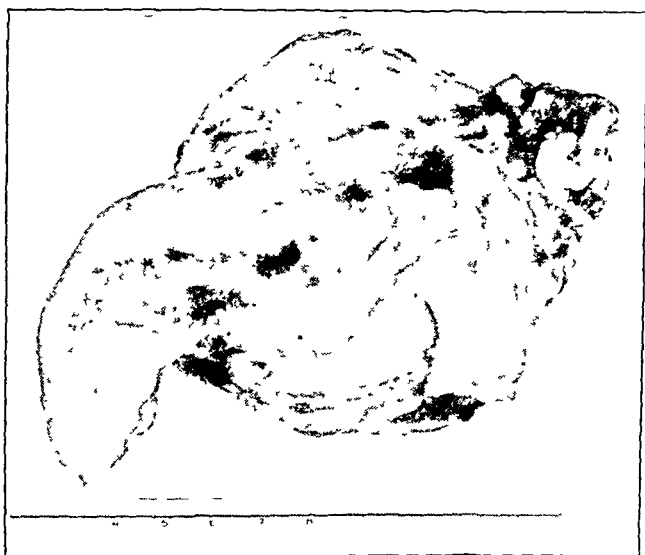


Fig. 1.—Appearance of cystlike dilatation of isolated loop shown attached to adherent normal intestine (in front). This occurred in an occasional animal when open ends of isolated loop closed spontaneously, allowing gradual distention of loop (see text).

it should be possible to determine whether in strangulation of the intestine the toxic effects are due mainly to the bacteria in the involved lumen or whether autolysis of the devascularized bowel is the main source of toxic substances. We therefore set out to determine the effect of "sterile" autolysis of the host's own intestinal tissue in the peritoneal cavity, using dogs.

Our first 17 dogs were prepared with the standard type of isolated loop of ileum as devised by Stone, Bernheim and Whipple.<sup>2</sup> The segment was washed out with saline solution and the ends allowed to

19. Laufman, H., and Method H      Unpublished data

remain open, essentially as Dragstedt, Moorhead and Burcky<sup>20</sup> had done. We found that with a successful anastomosis such animals would survive with no ill effects and the ends of the segment would gradually close over a period of four to six weeks. However, at the second operation, cultures taken from the center of such a loop invariably revealed a luxurious growth of mixed bacteria. Hence, with this method we were not able to produce "sterile" loops. Even when such animals were placed on a penicillin regimen, the loop yielded the same type of growth but in lesser amounts. An interesting feature of such animals was that the loop did not become distended, since the mucosal secretions drained freely into the peritoneal cavity until the time of spontaneous closure.

Occasionally, such a loop, some time after closure (four to six weeks after operation) would suddenly distend and even rupture, causing



Fig. 2.—Appearance of amputated loop which had become wrapped in omentum and had become revascularized (right). Normal bowel shown on left. This was prevented by amputation of omentum in later experiments (see text).

death of the animal from peritonitis. In a few instances, this distention was so gradual that the blood supply was not endangered and a cyst-like structure resulted (fig. 1). Although the organisms within such a loop or cyst were undoubtedly of low virulence, they were nonetheless present. The presence of bacteria became all the more evident by the sudden death of a few animals as late as five weeks following obstruction of the loop. In such animals autopsy showed distention and necrosis of the loop and peritonitis. It appeared that when there was dead or dying tissue on which to grow, the bacteria became pathogenic once

20. Dragstedt, L. R.; Moorhead, J. J., and Burcky, F. W.: Intestinal Obstruction: An Experimental Study of the Intoxication in Closed Intestinal Loops, *J. Exper. Med.* 25:421, 1917.

more. Our failure to produce sterile loops in which the bacteria would be incapable of returning to a state of virulence, therefore, caused us to alter our technic.

Another feature of these preliminary experiments was the striking observation that whenever the blood supply to one of these closed loops was severed and the loop placed back into the peritoneal cavity, it soon acquired a new blood supply through omental and serosal adhesions (fig. 2). This was especially true if the animal was protected with penicillin for the first few days postoperatively. The experiments of Sarnoff and Poth<sup>21</sup> in which a large segment of small intestine was deprived of its venous drainage after "sterilization" of the intestine

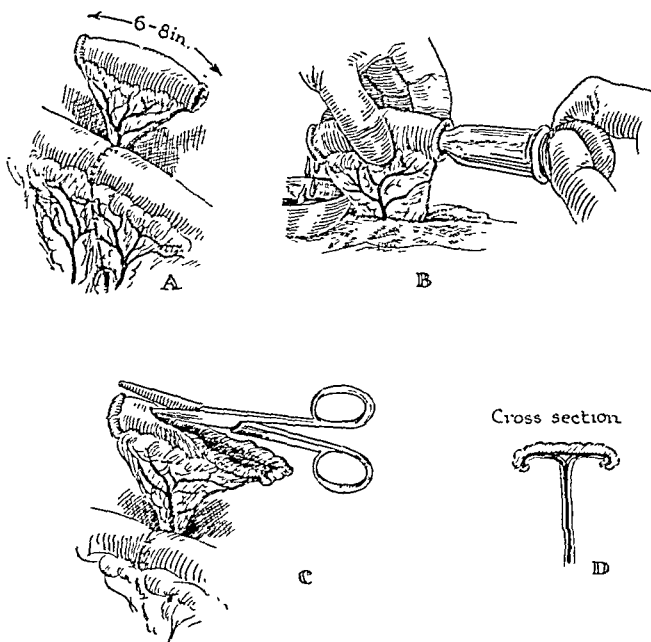


Fig. 3.—Technic of preparing open isolated intestinal loop (initial operation). *A*, segment of ileum removed from continuity allowing mesentery to remain intact; continuity of bowel reestablished by anastomosis. *B*, loop washed with sterile saline solution until washings are clear. *C*, segment cut open in its entire length. *D*, cross sectional appearance of open bowel with mesenteric attachment. At the second operation, several weeks later, the mesenteric pedicle is cut and the omentum is amputated.

with succinylsulfathiazole (sulfasuxidine®) indicated that such segments would survive in most instances when the bacterial count was low. More recently, Davis and associates<sup>22</sup> obtained similar results with

21. Sarnoff, S. J., and Poth, E. J.: Intestinal Obstruction: I. The Protective Action of Succinylsulfathiazole Following Simple Venous Occlusion, *Surgery* 16:927, 1944.

22. Davis, H. A.; Gaster, J.; Marsh, R. L., and Pritel, P. A.: The Effect of Streptomycin in Experimental Strangulation of the Bowel, *Surg., Gynec. & Obst.* 87:63, 1948.

streptomycin. Apparently, in each instance a new blood supply was formed from omental and serosal adhesions as well as from revascularization from the mesentery. The bowel in these experiments apparently never reached the stage of irreversible autolysis but, being almost sterile, was able to survive until a new blood supply was formed. These experiments, therefore, although indeed remarkable, did not demonstrate the effect of dead sterile intestinal tissue on the animal but did emphasize the importance of bacteria in such lesions.

Harper and Blain<sup>23</sup> placed penicillin into isolated closed loops and found that it protected the animal and prolonged life. Later, Blain<sup>24</sup> used penicillin in strangulated low ileal obstruction, together with whole



Fig. 4.—Appearance of devascularized intestine three weeks after second operation. Note gelatinous appearance of partially autolysed tissue

blood and isotonic sodium chloride solution, to combat shock, hemorrhage and loss of chloride and water. He found that such animals lived considerably longer than did the similarly treated controls without penicillin and that resection could be delayed with successful results.

There seems to be little question that bacteria are important in the toxic features of strangulation obstruction, but the isolated effects of sterile autolysis of dead intestinal tissue have apparently not been adequately demonstrated.

23. Harper, W. H., and Blain, A.: The Effect of Penicillin in Experimental Intestinal Obstruction, *Bull. Johns Hopkins Hosp.* 76:221, 1945.

24. Blain, A.: Penicillin in Experimental Intestinal Obstruction, *Surg., Gynec. & Obst.* 84:753, 1947.



Fig. 5.—Microscopic appearance of devascularized intestine shown in figure 4. There is intense polymorphonuclear infiltration of all layers, and the muscularis shows early degenerative changes.

## TECHNIC AND RESULTS

In order to satisfy the requirements of an experiment which would obviate the criticism of previous work done in this field, the following were our aims: (*a*) to isolate a segment of appreciable length of the dog's own intestine; (*b*) to devise a means whereby such a segment would become free of pathogenic organisms; (*c*) to sever the blood supply to the segment, and (*d*) to allow the segment to remain in the host's own peritoneal cavity without acquiring a new blood supply, yet permitting peritoneal absorption of any toxic substances which might result.

In 21 dogs a 6 to 8 inch (15 to 20 cm.) loop of the lower part of the ileum was isolated from its continuity and anastomosis created around it. Its blood supply for



Fig. 6.—Appearance of devascularized intestine six weeks after second operation. The noodle-like remnant is partially adherent to a normal loop of intestine.

the present was left intact. The loop was washed out with sterile isotonic sodium chloride solution and cut open in its entire length on the antimesenteric border (fig. 3). The abdomen was then closed. Fourteen animals survived with no apparent ill effects. Of the 7 deaths, 3 were the result of a leaky anastomosis with peritonitis, while 4 resulted from torsion of the mesenteric pedicle with strangulation of the isolated strip. The latter group will be discussed later.

At the second operation, performed on the 14 surviving animals six to eight weeks later, many adhesions were found about the segment and there was considerable mucus entrapped in these adhesions. In several of the animals the exudate was caseous in character. At this operation the segment was cut free of its mesenteric blood supply and of all adhesions and literally lifted free from the animal. The omentum was then amputated so that it could not give the segment a new blood

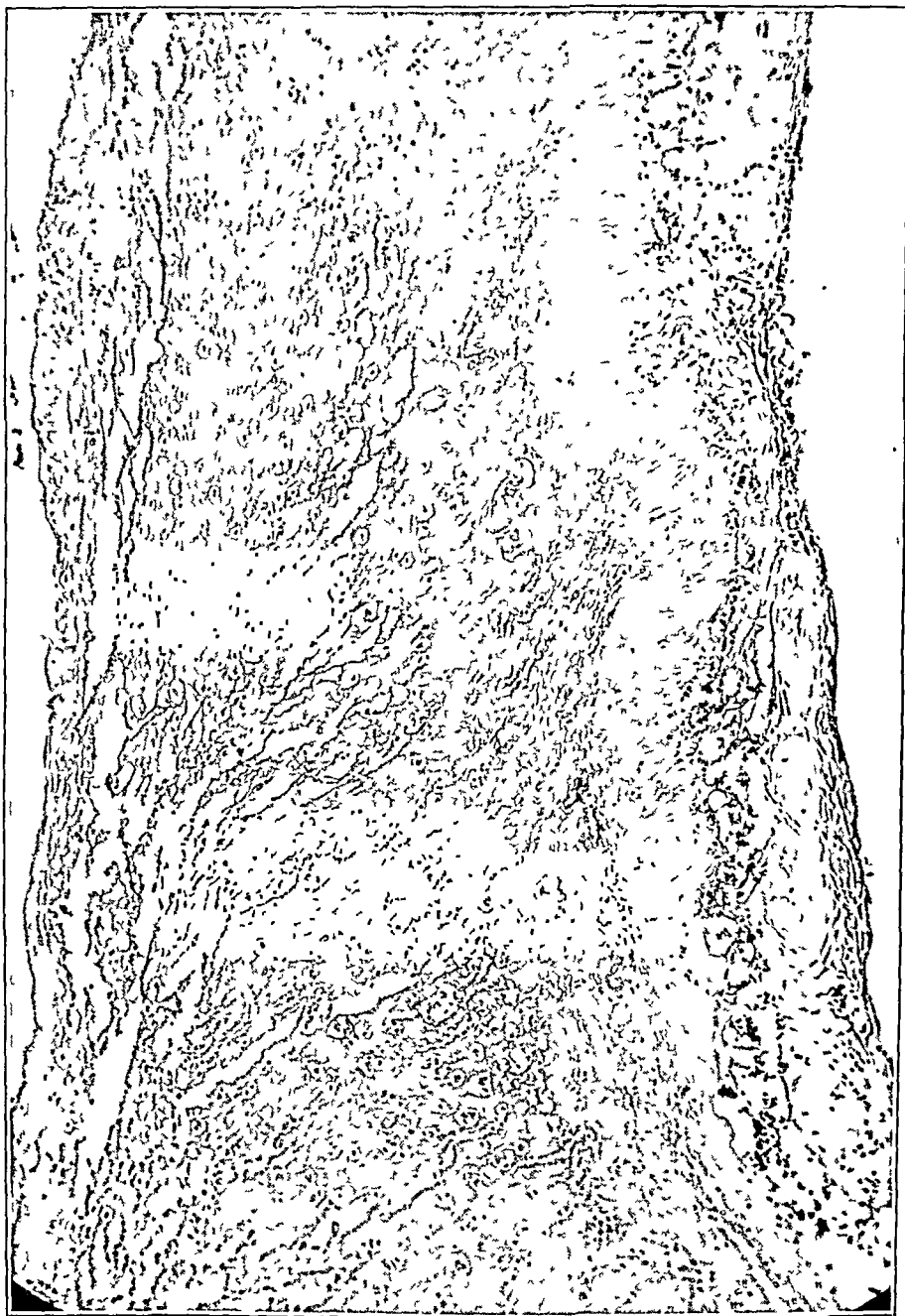


Fig. 7.—Microscopic appearance of devascularized intestine shown in figure 6. Note almost complete degeneration of mucosa. Nuclei in muscularis are pyknotic and surrounded by vacuoles. Muscle fibers in some areas are no longer discernible, leaving only ghost structures.

*Organisms Obtained from Tissue Cultures*

Dog No.	Culture Taken from Tissue at Second Operation (Blood Supply Intact) Six to Eight Weeks After First Operation	Culture Taken from Tissue at Third Operation (Blood Supply Severed) Three to Fourteen Weeks After Second Operation
19.....	<i>B. tritus</i>	.....
25.....	<i>Erysipelothrix</i> (species undetermined)	.....
26.....	<i>B. subtilis</i>	No growth
27.....	No growth	No growth
28.....	No growth	No growth
29.....	No growth	<i>B. aerogenes</i>
30.....	<i>Strep. faecalis</i>	.....
31.....	<i>E. coli</i> <i>Strep. viridans</i> <i>Staph. albus</i>	<i>E. coli</i>
33.....	<i>E. coli</i> <i>Actinomyces</i> (species undetermined)	<i>E. coli</i>
35.....	<i>Strep. faecalis</i> <i>E. coli</i>	No growth
37.....	<i>E. coli</i> <i>Staph. albus</i>	<i>Staph. albus</i>

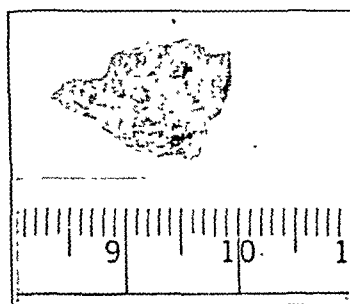


Fig. 8.—Appearance of devascularized intestine eight weeks after second operation. This pea-sized nodule was removed from its attachment to the parietal peritoneum for purposes of photography. Rim of peritoneum can be seen surrounding specimen.

supply by enveloping the segment after it was replaced. Cultures taken from the tissue in 11 different animals at this time (the table) revealed various bacterial forms in 8. These forms were among those commonly found in the intestinal contents. In ordinary circumstances they can assume a pathogenic role only when introduced into the peritoneum from the lumen or when they can propagate on a substratum of dead tissue. In 3 instances there was no growth of bacteria on the culture mediums. We considered such a piece of tissue as "bacteria-free" as it was possible to get in the dog with use of ordinary aseptic surgical technic.

The strip of intestinal tissue was then reimplanted into an adhesion-free portion of the peritoneal cavity, and the abdomen was closed. All but 2 of these animals were treated with penicillin for three days



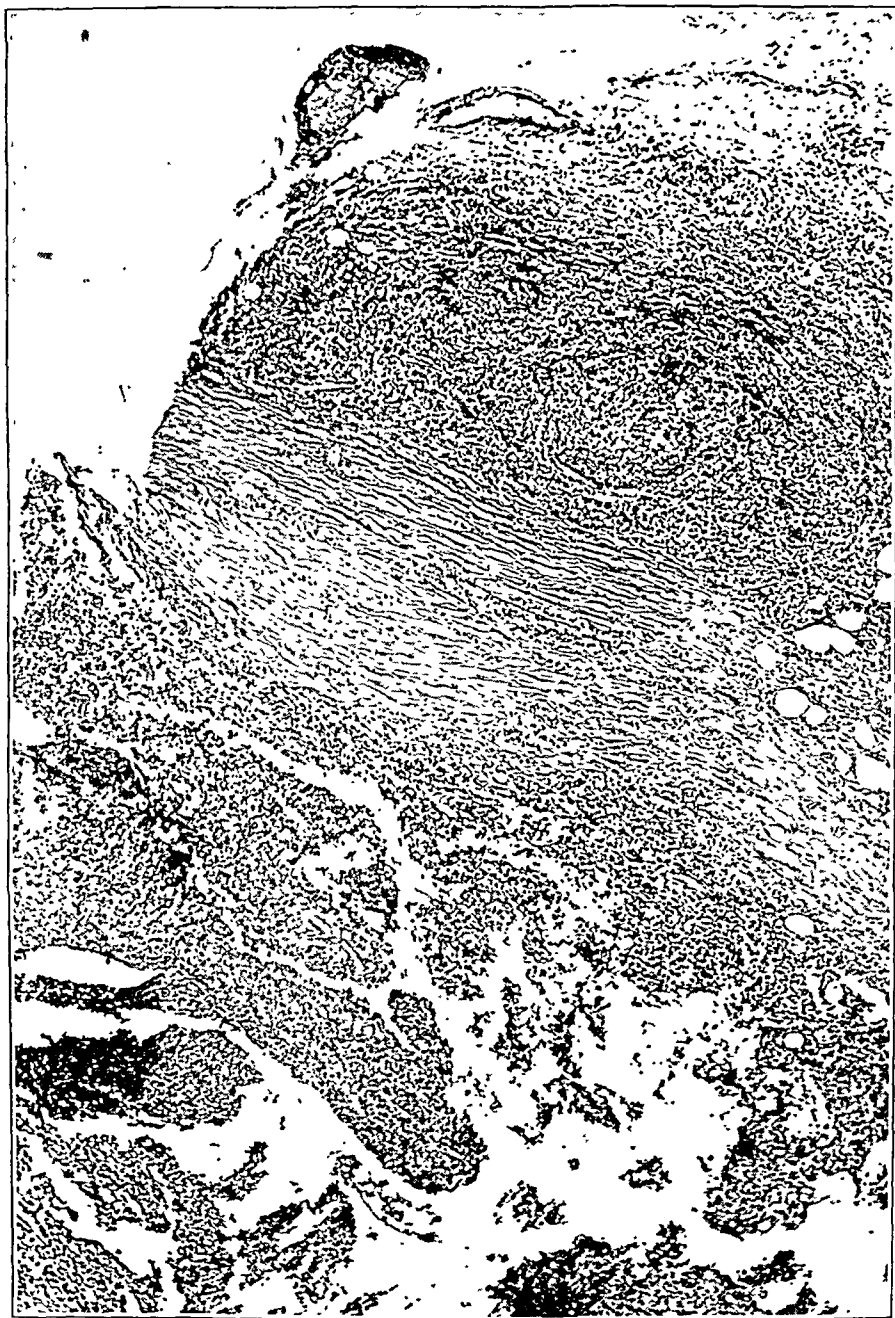


Fig. 9.—Microscopic appearance of devascularized intestine shown in figure 8. Changes are essentially those described in figure 7.

in an attempt to counteract any pathogenic bacteria which may have been present or introduced by the surgical procedures. In the 2 instances in which penicillin was not employed (dogs 27 and 28) the cultures revealed no bacterial growth. After the second operation the animals were watched for periods up to three months. In no instance did any of them show gross signs of distress. On the contrary, many gained weight and all appeared perfectly healthy.

The third operation was then done to expose and examine the area in which the segment was placed (usually the right upper posterior portion of the peritoneal cavity). Cultures taken at this time from 8 animals (the table) revealed no growth in 4 of them. In the remaining 4, the organisms found were *Escherichia coli* in 2 instances, *Staphylococcus albus* and *Aerobacter aerogenes*.

This operation was performed from three to fourteen weeks after the previous laparotomy. At three weeks the tissue presented a gelatinous appearance (fig. 4). At six to eight weeks (in other animals) the tissue no longer bore any gross resemblance to intestinal tissue. In some cases there remained only a thin white strand, similar in appearance to that of a cooked noodle (fig. 6). In other instances the implanted tissue appeared as a small plaque, no larger than a pea, partially adherent to a loop of small intestine or parietal peritoneum (fig. 8). At ten to fourteen weeks (in other animals) only tiny bits of tissue remained, and in 1 animal an exhaustive postmortem search revealed no trace of the tissue except for an almost insignificant adhesion at the site at which it was thought the tissue had been implanted.

#### COMMENT

These results give us the impression that we have demonstrated that the intraperitoneal autolysis of the host's own intestine in the relative absence of pathogenic bacteria produces no observable deleterious effect on the animal. The technic of graded operations resulted in a progressive diminution in bacterial forms. After the first operation, in which the blood supply was left intact and a large portion of the bacteria were removed by the washing technic, the natural defense mechanisms were able to protect against the invasion by opportunists. At this stage the integrity of the blood supply appeared to be the crucial issue, since when it became endangered by torsion of the mesenteric pedicle the otherwise harmless bacteria were able to propagate on the substrate of dead or dying tissue and cause death.

By the time the second operation was done, the tissue was either free of bacteria or contained only a few remaining bacterial forms. Deliberate severance of the blood supply at this time therefore caused no ill effects, especially since added protection against the remaining opportunists was afforded by a three day course of penicillin.

If it may be inferred that the autolysis of sterile dead tissue *in vivo* is nontoxic, the natural conclusion would be, therefore, that the toxicity is due entirely to bacteria. On the other hand, the picture is not one of septicemia, as evidenced by our preliminary work and that of others on the nature of the pathologic physiology. Whether the toxicity of autolysis in the presence of bacteria arises from the action of bacteria, bacterial endotoxins, bacterial exotoxins or other spreading factors in the presence of dead tissue cannot be stated with finality at this time, especially since it has been shown recently that penicillin and its impurities offer protection against certain bacterial endotoxins.<sup>25</sup> In the 2 cases in which we did not use penicillin there was no growth on culture, and therefore these cases offer no further information.

We conceive that when the bacteria have a substratum of dead or dying tissue on which to act the combination results in the release of spreading factors which contributes to a state of local and generalized increased capillary permeability, thus contributing to the toxic state. Further, we believe that the release of polypeptides from tissue autolysis is of no consequence unless bacteria are present in sufficient concentration or virulence. If these premises are allowed, it would appear that the toxicity of tissue autolysis is enhanced by the local invasion of bacteria and that the toxicity of the local invasion of bacteria is enhanced by tissue autolysis. Thus the integrity of blood supply is just as crucial as is the bacterial incubation, despite the fact that sterile tissue autolysis is innocuous. Our impressions tend to conform with those originally set forth by Dragstedt.<sup>5</sup>

At the present time we are conducting experiments in this laboratory with the hope of further clarifying the spreading factors. This problem is being approached from the standpoint of enzyme chemistry.

#### SUMMARY

We have devised a means of demonstrating the effects of autolysis of devascularized intestine in the host's peritoneal cavity in the relative absence of pathogenic bacteria. Our observations indicate that a strip of devascularized ileum will undergo almost complete autolysis in the peritoneal cavity of the dog with no ill effects on the animal provided the tissue is relatively bacteria free. We feel that the implication of this finding is of some importance in the search for toxic factors in intestinal strangulation and allied conditions.

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25. Miller, C. P.; Hawk, W. D., and Anderson, W. H.: Protection Against Bacterial Endotoxins by Penicillin and Its Impurities, read before Society of Illinois Bacteriologists, Peoria, Ill., Oct. 15, 1948.

# USE OF AN ABDOMINAL FLAP GRAFT IN CONSTRUCTION OF A PERMANENT ILEOSTOMY

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AND

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THE PATIENT who must have a permanent ileostomy has been materially benefited by the technic of Dragstedt and his associates,<sup>1</sup> who covered the terminal ileum with a split thickness of skin, thus providing a greater length of bowel externally and facilitating the collection of fecal material into a suitable container.

The inherent tendency, however, of both the bowel and a split thickness graft to contract may, over a period of time, result in a marked shortening of the ileostomy. In 1 patient for whom we made such an ileostomy, the original 3½ inches (9 cm.) of skin-covered ileum over a period of eighteen months contracted to the point that only ¼ inch (0.6 cm.) of skin remained and the mucosal edges of the bowel were in contact with the skin of the abdomen. This occurred in spite of a primary take of the graft. There would undoubtedly be less contraction with a thicker graft.

It occurred to us that if one were to utilize a full thickness flap graft containing fat, fascia and its own blood supply the resistance of the skin bordering the ileostomy stoma would be much greater and the possibility of later contraction practically eliminated.

When a patient with familial polyposis involving the entire colon presented himself, the following technic was carried out.

## OPERATIVE PROCEDURE

Through a right upper paramedian incision, the terminal 6 inches (15 cm.) of ileum, the right colon and half to two thirds of the transverse colon were resected. The distal 5 inches (13 cm.) of remaining ileum, the opening of which had been closed with a purse string, were then mobilized by severing the vessels just below the distal arches. The viability of the bowel remained intact. A flap of skin was next outlined and elevated (fig. 1) in the right lower abdominal quadrant, the base

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From the Department of Surgery, Veterans Administration Hospital, Hines, Ill., and the Presbyterian Hospital, Chicago.

1. Dragstedt, L. R.; Dock, G. M., and Korsner, J. B.: Chronic Ulcerative Colitis: A Summary of Evidence Implicating Bacterium *Necrophorum* as an Etiologic Agent, *Ann. Surg.* **114**:653-662, 1941.

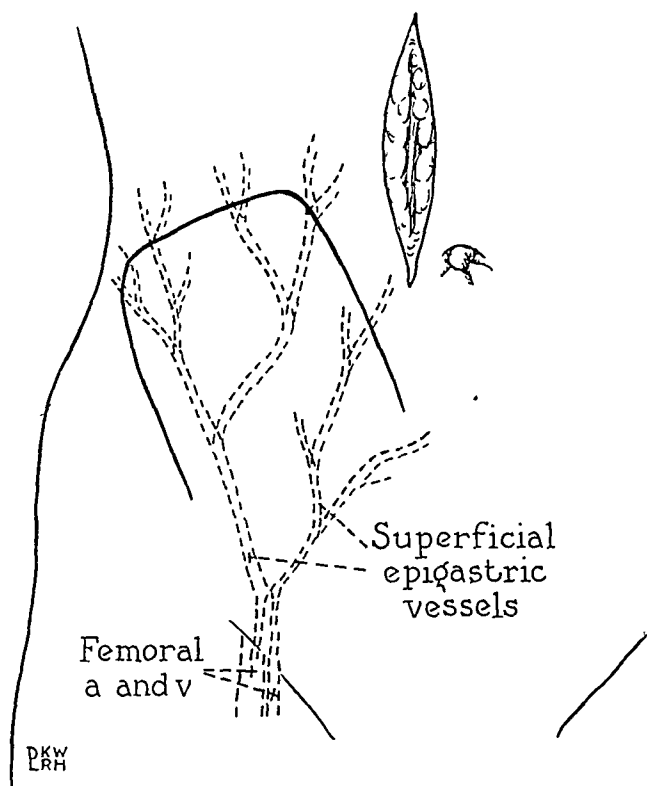


Fig. 1.—Outline of flap on the abdomen, showing distribution of principal blood vessels.

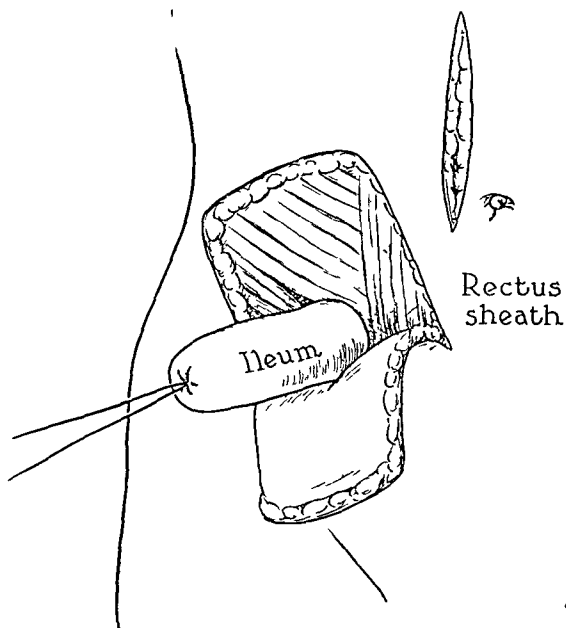


Fig. 2.—The flap has been elevated and the distal end of the ileum brought through a muscle-splitting incision just above the base of the flap.

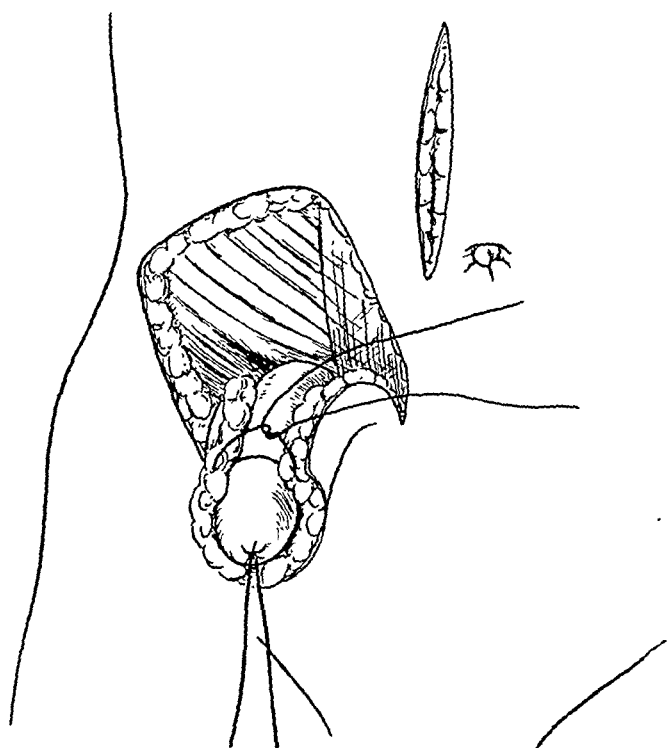


Fig. 3.—The flap is being wrapped about the bowel, and the fascia is closed to itself by suture.

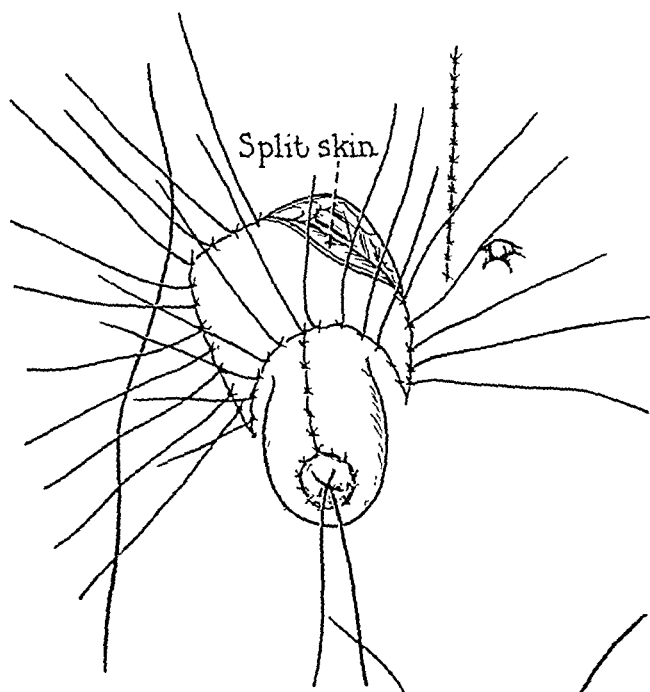


Fig. 4.—The flap has been wrapped about the ileum and sutured to itself on the dorsal aspect. The serosa of the bowel has been sutured to the skin of the flap at its distal open end. The donor site of the flap is covered with a split thickness skin graft.

being directed downward. The flap was approximately 4 inches (10 cm.) in length,  $3\frac{1}{2}$  inches (9 cm.) wide and consisted of skin, subcutaneous tissue and fascia with the vessels contained therein. When completely lifted, it appeared to have an adequate blood supply. A muscle-splitting incision was then made through the abdominal wall (fig. 2) just above the central portion of the base of the flap and the ileum brought through this wound. The skin flap was then wrapped about the ileum (fig. 3) and the skin edges approximated, interrupted sutures of fine surgical gut being used in the subcutaneous tissue and nylon sutures in the skin. The mesenteric border of the ileum lay parallel to this suture line. The ileostomy was not opened, and its serosa was sutured directly to the skin edges about the distal end of the newly constructed tube.

The donor site of the flap on the lower right side of the abdomen (fig. 4) was covered with a split thickness skin graft from the anterior aspect of the right thigh.

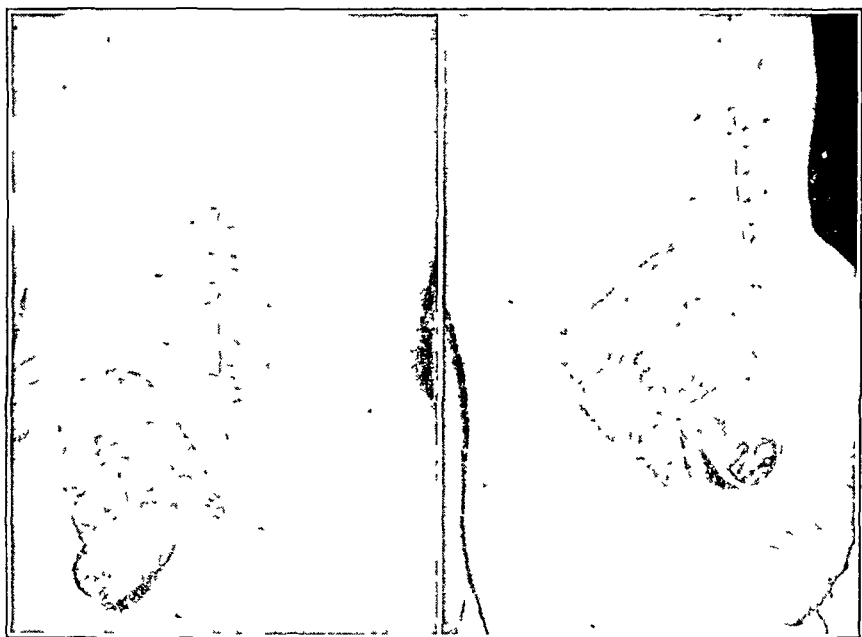


Fig. 5.—Appearance on the eleventh day after ileostomy. The major portion of the split thickness graft in the donor site of the flap has taken well. It is to be noted that a small slough of the margin of the ileum has not yet completely separated to leave a skin-mucosa junction.

This graft was immobilized by tying the sutures, which were left long, over a stent of nylon fabric and moist cotton. The newly made ileostomy was a penile-like structure standing on the abdominal wall about  $2\frac{1}{2}$  inches (6 cm) high. The paramedian incision was then closed and the entire abdomen dressed with a soft bulky pressure dressing which was adequately built up about the ileum and its skin cover to prevent undue pressure.

The ileostomy was not opened at this time but was covered with sufficient dressings generously spread with zinc oxide ointment to protect against spontaneous opening and consequent contamination of the split thickness skin graft. Prior to the operation a Harris tube had been passed well into the lower part of the ileum. The patient was allowed to take water by mouth, and his nutrition was maintained by intravenous administration of fluids. The ileostomy remained closed for seven days following the operation.

The dressing was removed from the split skin graft on the eighth postoperative day, and it was found to have taken almost completely. Subsequently, three or four small areas within the graft broke down (fig. 5), but these healed promptly and the wound has remained clean. There was, naturally, some sloughing of the wall of the ileum at the point where it was sutured to the skin of the flap. When this excess mucosa and bowel wall had sloughed, the skin of the flap and the mucosa formed a fine line of union (fig. 6). The ileostomy stoma now rested about 2 inches (5 cm.) beyond the abdominal wall.

#### PROSTHESIS FOR COLLECTION OF BOWEL CONTENTS

Any contact of ileal contents with the skin may result in excoriation of the latter, and, even though the intestinal contents drop into a bag

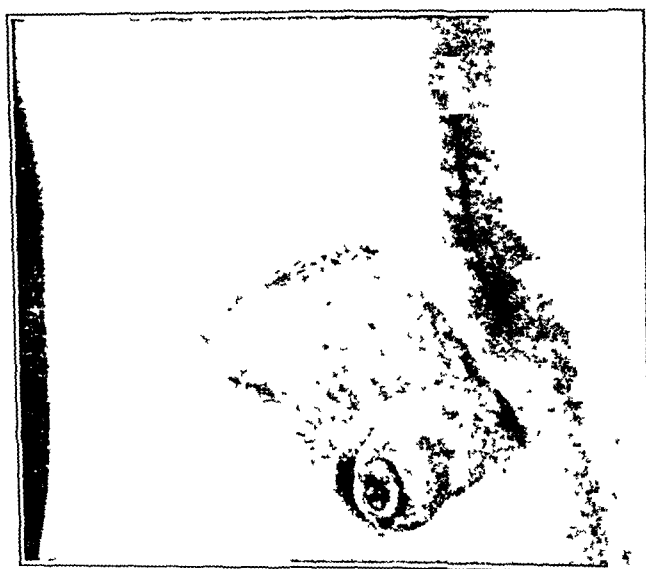


Fig. 6.—Condition about eight weeks after ileostomy. The mucosa extends beyond the skin just far enough to permit the easy fitting of the ileostomy cup (shown in figure 7) and thus prevents contamination of the skin with feces

from a length of ileum, there is likely to be irritation of the skin near its junction with the mucosa.

With the help of Drs. Paul E. Richards and Robert E. Peters, of the Prosthetics Department of the Veterans Administration Hospital, Illinois, Ill., we have devised a prosthesis which has met in part the requirements of a satisfactory "ileostomy cup."

The prosthesis consists of a basic form of sponge latex molded to the abdomen for a radius of approximately 7 cm. about the ileostomy and painted with three layers of pure latex to seal the pores (fig. 7). A firm acrylic resin mold is annealed over this, and at its peak there is a rounded cuff about 4 cm. in diameter (fig. 8). A rubber bag about 20 cm. in length snaps over the rim of the cuff and is held



in place by its own elasticity. The cuff has a solid floor except for an opening in the center which admits the mucosa only. The edge of this opening is lined with soft sponge latex to eliminate pressure on the mucous membrane and fits



Fig. 7.—Ileostomy cup constructed by the prosthetics department of the Veterans Administration Hospital. The outer hard frame is made of firm acrylic resin, and the inner core which fits about the ileostomy is sponge latex covered with pure latex to seal its pores and prevent soiling.

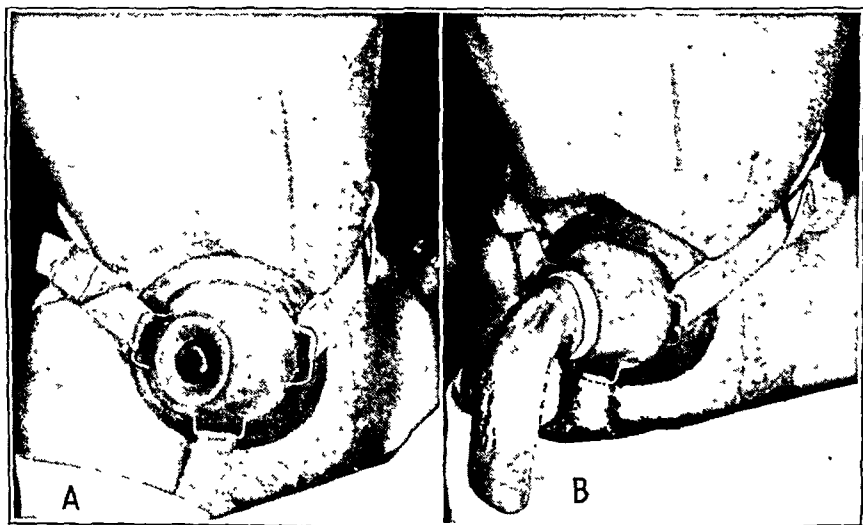


Fig. 8.—Ileostomy cup in place without (A) and with (B) disposable latex bag for the collection of fecal material.

closely about the mucosal edge. The floor of the hard plastic cuff is about 8 mm. below the rim. In order to keep the mucosal opening in place, the ileostomy is supported with cotton, wrapped about its base before the prosthesis is set in place.

A little zinc oxide ointment over the skin at its junction with the mucosa serves to seal the opening in the prosthesis. The appliance is held in place by a strap around the trunk and another through the groin.

During a peristaltic wave the ileostomy becomes relatively rigid and the stoma is forced against the prosthesis, acting further to maintain the seal and prevent soiling of the skin. The rubber bags are made by painting multiple layers of latex over plaster forms, and the patient carries a small supply for change and disposal at will.

The consistency of the ileostomy four months after its construction is that of a relaxed penis. It may be pulled from the abdominal wall 1 to 2 inches (2.5 to 5 mm.) beyond its apparent length. Such manipulation allows the patient to stimulate peristalsis at will and

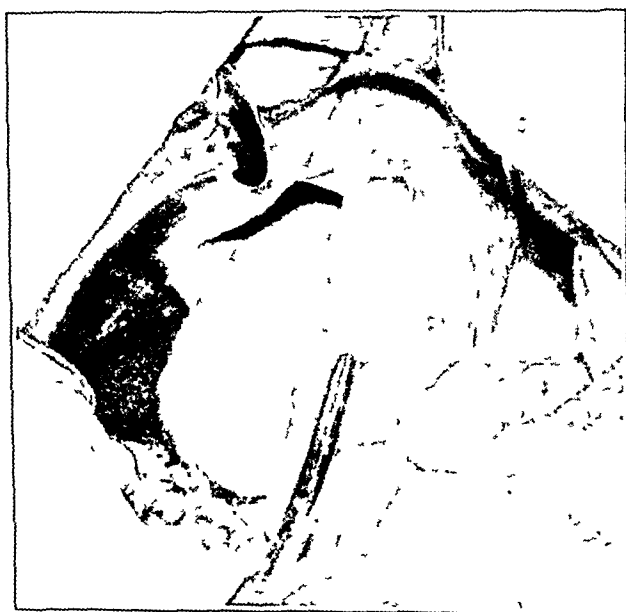


Fig. 9.—Photograph taken during the second operative procedure for removal of the remaining portion of the colon. The distal ileum is shown to have dilated to form an ampulla-like pouch in response to the loss of the colon.

empty the newly formed ampulla-like pouch of the lower part of the ileum (fig. 9), which was found to have developed when the second operation for removal of the remainder of the colon was performed. He has thus been able to halt the flow of intestinal contents for periods up to four hours, and it is hoped that the need for any kind of cup may eventually be eliminated. Certainly, the care of this ileostomy seems little more bothersome than that of the usual colostomy at four months.

#### COMMENT

Plastic surgeons and surgeons working on the hand have for years appreciated the valuable blood supply found in the broad-based

flaps from the abdomen. Shaw<sup>2</sup> has written an excellent description of the technic as applied to injured hands. The course of the superficial epigastric artery and vein as they come off the femoral vessels and pass upward in the skin and fascia of the abdominal wall assures an adequate blood supply to this area of skin. Except as the skin may be altered by scars, there is little reason to expect difficulty with the nourishment of such a flap. In the procedure here described the suture line of the flap must, by virtue of the course of the blood supply, lie on the dorsal surface of the tube. As a result, there may over a period of time be a tendency for the tube to be drawn dorsally. Such contraction may need correction by a Z-plasty, but there are adequate skin and subcutaneous tissue to allow such a procedure.

While this is not an overly laborious or time-consuming procedure, it seems to us that it should not be used when the patient is not in reasonably good condition. A patient who is acutely and severely ill with ulcerative colitis should not have this type of stoma constructed when ileostomy is being performed as an emergency and oftentimes life-saving procedure. The success of this procedure will depend on good wound healing, which the severely ill patient will seldom demonstrate. However, when an emergency ileostomy is done, it would be to the patient's advantage to have the opening placed near the midline so that the skin of the right lower quadrant would not be molested and thus be available for later use in revising the ileostomy along the lines described.

Though we have not had an opportunity to carry out such a procedure, we feel that in many cases in which the conventional ileostomy has already been made in the right lower quadrant, it would be possible to mobilize the ileum sufficiently to accomplish this operation in the left lower quadrant.

#### SUMMARY

A technic is described for constructing a permanent skin-covered ileostomy by wrapping the terminal ileum in a flap of skin, subcutaneous tissue and fascia, nourished primarily by the superficial epigastric vessels.

A suitable prosthesis has been devised which fits such an ileostomy and provides for satisfactory collection of bowel contents.

#### DISCUSSION OF PRECEDING PAPERS

DR. HAROLD LAUFMAN, Chicago: I should like to comment on the excellent work done by Drs. Hill and Saltzstein and their group. I have had some laboratory and clinical experience with tetraethylammonium chloride. When a vasodilating drug such as this is used in a patient with vascular occlusion, one logically expects

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2. Shaw, D. T., and Payne, R. L., Jr.: One Stage Tubed Abdominal Flaps; Single Pedicle Tubes, *Surg., Gynec. & Obst.* **83**:205-209, 1946.

local dilatation to result. This is not always the case. Therefore, one is entitled to ask: Should I use the drug, or shouldn't I? Is it good or is it bad? Will it do harm, or will it do nothing? Tetraethylammonium is an interesting drug because it does some of all these things. It is both good and bad. The Michigan group, responsible for much of the preliminary pioneering work with this drug, has obtained therapeutic results in many forms of peripheral vascular disease as well as in hypertension. Their work with the drug in hypertensive patients has indicated that the more precarious the hypertension the greater the effect of the drug (Lyons, R. H.; Moe, G. K.; Neligh, R. B.; Hoobler, S. W.; Campbell, K. N.; Berry, R. L., and Rennick, B. R.: Effects of Blockade of Autonomic Ganglia in Man with Tetraethylammonium, *Ann. J. M. Sc.* **213**:315 [March] 1947). From these observations they formulated the concept that the greater the stimulation in the sympathetic ganglions, the greater would be the blocking effect of the drug.

In our work we found that this concept could not apply to the type of local ganglionic stimulation which results from acute vascular occlusion (Martin, W. B.; Laufman, H., and Tuell, S. W.: Rationale of Therapy in Acute Vascular Occlusions Based Upon Micrometric Observations, *Ann. Surg.*, April 1949). As a matter of fact, we found that no generally acting drug was capable of releasing local stimulation in sympathetic ganglions to the extent that was obtained by local procaine block. We were, therefore, delighted when Dr. DeBakey's article appeared (DeBakey, M. D.; Burch, G.; Ray T., and Ochsner, A.: The "Borrowing-Lending" Hemodynamic Phenomenon [Hemometakinesia], *Ann. Surg.* **126**:850-865 [Dec.] 1947), in which his group reported similar results.

We have arrived at a concept concerning the action of tetraethylammonium chloride in peripheral vascular occlusions which I should like to present. The concept set forth by the Michigan group is apparently tenable when the sympathetic tonus throughout the entire body is of almost equal magnitude, but it requires revision when it is applied to local vascular occlusions. We conceive that the drug by acting on all ganglions in the body has a lesser effect on those ganglions harboring a powerful stimulus from an occlusive irritant than it has on normal ganglions. This, in effect, would be a distribution of the action of the drug along "paths of least resistance." Thus, in an instance of acute vascular occlusion, the action of the drug would dissipate itself throughout the body without being able to "break through" the area in which it was most needed. If its action resulted in a general drop in blood pressure, a harmful effect could result in the area already suffering from a diminished blood supply. Also, if the drug is injected too rapidly and a lowering of the blood pressure ensues, the same effect may result. This was reflected in our measurements by a diminution in caliber of already spastic vessels.

Our concept is borne out by the experiences of Dr. Saltzstein's group in their intestinal experiments. When the bowel was strangulated or when the area was otherwise stimulated, the drug actually resulted in a lowering of the temperature of the involved area, or a reversal of effect, so to speak.

It is known that in acute occlusions of the extremity or in stimulations of ganglions due to acute pain, the drug will cause either no effect on that limb or an actual drop in temperature. We interpret this reversal of effect as a dissipation of the drug among unstimulated ganglions, and because of the principle of hemometakinesia, blood is actually drawn away from the local area and the local temperature drops.

However, in instances in which there is a collateral blood supply and that collateral blood supply comes from a higher area innervated through another ganglionic level, the drug will affect such collaterals by dilating them and pro-

ducing an increased blood supply to the part. The drug is not able to produce new blood vessels, but when vessels are present they can be dilated provided the circumstances just described exist. This apparently was the situation in the occlusion experiments of the aorta which were presented here. I understand some of the successful experiments were in pregnant bitches which had a large collateral blood supply to the lower extremity. In such instances it certainly is conceivable that the drug resulted in sufficient dilatation of the collateral vessels to result in a decent blood supply to the lower extremity.

I should like to hear some other comments from some of you here. What I have related is simply the result of our experience with this drug and the application of our concepts to explain what otherwise would seem to be paradoxical results. I should like to commend the work of this group in performing these experiments, because I think it is important to realize the limitations of any drug.

DR. J. T. REYNOLDS, Chicago: I should like to make a remark about the paper by Dr. Patton and Dr. Johnston concerning the treatment of hemorrhage from esophageal varices. Our problem has been that of treating a patient properly who was actually bleeding to death under our eyes. One can avoid the patients and say they are too sick for treatment, but such an attitude is not commendable. Patients who are bleeding actively should not be subjected to the operation of portocaval shunt during their hemorrhage because they are in poor condition and cannot tolerate such operation. Obviously, the use of the balloon that Dr. Patton suggested has very many merits. Unfortunately, we have not yet had the opportunity of using their tube. We used a tube with a balloon on it which we manufactured ourselves, and it was not effective. At operation we found that the patient continued to bleed after we had inflated the balloon, because the balloon had dropped down in the patient's stomach.

I was glad to hear the suggestion of adding thrombin above the large balloon because we have found that in some of our patients bleeding from gastric cancers the use of thrombin was distinctly helpful. It is probable that patients who are bleeding actively can be treated with this balloon tube until bleeding has stopped. After the bleeding has stopped and the patients are in better condition, the definitive portocaval shunt should be done.

From Dr. Julian's paper this morning, I think it is apparent that very soon we will have some sort of device that will be satisfactory to allow us to do portocaval shunt very safely. This of course presumes a patient who is in good condition.

DR. MAX M. ZINNINGER, Cincinnati: I should like to make just a few remarks about the paper by Dr. McClure and Dr. Brush on islet cell tumors in the pancreas. I have not had a wide experience with these, but they are very spectacular tumors, as he has indicated. For instance, in 1943 I saw a patient in her sixties, who was admitted to the hospital in coma. She was first thought to have a brain tumor because of the coma. It was finally learned that her blood sugar was 23 mg. per hundred cubic centimeters and it was found that the only way she could be kept out of coma was by putting a tube into her stomach and giving her glucose solution continuously. She was operated on, and a tiny tumor, less than 1 cm. in diameter, was easily found in the head of the pancreas, and removal of the tumor entirely cleared up her abnormal glucose metabolism. However, her brain was permanently damaged as a result of the continuous insulin shock.

In contrast, I should like to point out that some of these cells do not produce insulin at all. For example, in 1941 I operated on a rather large tumor of the

pancreas, which measured 6 by 8 by 12 cm. after fixation. This patient showed no abnormal glucose metabolism. Careful study of the tissue showed that the cells contained no alpha or beta granules but only delta granules, and that type of islet cell apparently does not produce insulin. This patient died in 1943, and there was widespread metastasis of tumor which was comparable in appearance to the original tumor.

DR. JAMES T. PRIESTLEY, Rochester, Minn.: I think, as we have just heard from the last discussor, that the patients who have hyperinsulinism constitute a very interesting group, and operation on these patients can be satisfactory and simple or rather difficult and disappointing.

If there is a single adenoma found, ordinarily it can be enucleated without much difficulty, and the patient gets along quite well. On the other hand, sometimes one can search from the tail to the head of the pancreas and back again two or three times and not find anything in the way of a tumor. Usually in those circumstances there is a small lesion embedded within the gland, of the same consistency as the pancreas, and even though one may visualize it by making an incision in the pancreas, it may be the same color as the normal pancreas and very difficult to recognize. I recall an instance when a portion of the pancreas was removed for such a lesion, and the pathologist brought the specimen back and said there was no tumor, having made a number of sections through the pancreas, but further search did reveal the tumor.

I think that there are one or two points that might be mentioned. In the first place, these tumors can be multiple. The incidence of multiple adenomas of the islands of Langerhans is quite small, but just because one is found in a certain portion of the gland does not mean that further search should not be made for another adenoma. We have had 1 patient in whom a malignant adenoma, a functioning tumor, of the islands was removed, and the patient was relieved, but he subsequently returned with recurrent symptoms of hypoglycemia and there were metastases.

Perhaps you would be interested in the patient referred to, in whom we did total pancreatectomy six or seven years ago. This patient is alive and leading a normal life today. About a year ago, which was approximately five and a half years after operation, we had the opportunity to study her in the metabolic unit, and, in contrast in some ways with the experimental animal, she showed no evidence of decreased liver function by any of the currently employed tests, despite the fact that she had not taken substitution therapy of any kind. She did, of course, show marked lack of internal and external pancreatic function, in that she required between 20 and 25 units of insulin a day, and the percentage of undigested fat and protein in the stool was abnormally high.

DR. JOHN R. PAINE, Buffalo: Will Dr. Laufman tell us a little of the details of the regimen and how long he followed the regimen in making these sterile devascularized intestinal loops?

DR. H. M. ELDER, Montreal: I was greatly interested in Dr. Thieme's review of appendicitis and still more interested in the fact that he gives a great deal of credit to the use of sulfonamides. I think that perhaps is an attitude of mind which we should not permit ourselves always to drift into. It is so easy to credit any improvement to the antibiotics and then, perhaps, to neglect some of the other things. I was not quite clear as to how the sulfonamide was used, whether it was used in intraperitoneal implant or not. I should like information on that point. My own experience has been that the intraperitoneal sulfonamide implant has proved very disappointing in that it tends to be a bit of an irritant. I have

not been able to satisfy myself that the actual concentration of antibiotic locally was effective against organisms. I wonder whether possibly the change in the operative technic he mentioned, the changes which have come about over the ten year period in preoperative and postoperative care of patients, may not have more to do with the gratifying lowering of his mortality figures than the actual sulfonamide therapy.

DR CHARLES G. JOHNSTON, Detroit: I want to say a word in relation to the point which Dr. Reynolds brought out. I doubt that Dr. Patton made it clear. In the case which he reported operation was not done shortly after the patient was bleeding. We used the same principle in stopping the bleeding. It is purely a temporary measure. Its use is primarily that of stopping the blood. It is purely a matter of applying pressure on the dilated veins. What is done afterward is another problem. It is really a matter of tiding the patient over until something else can be done. Usually we feel that a portocaval shunt or some type of shunt which will reduce the pressure in the portal system is the ideal form of therapy if it is possible to do that afterward. As a matter of fact, so far as we are concerned, bleeding from the esophageal varices is the best indication and the most obvious indication for portocaval shunt.

DR. EDWIN M. MILLER, Chicago: I wonder whether as a result of these injection experiments of Dr. Noer, in which after tying off the main artery as well as the arcades and the vasa recti the segment of bowel becomes filled with dye via the anastomotic vessels within the bowel wall, he could draw any conclusions which would in any way materially affect our standard procedures used in performing an end to end anastomosis of the intestine. After all, what we rely on after tying off the main vessels to a loop to be resected is the color changes in the bowel wall in order to determine where we can safely plan our lines of suture.

DR. BROCK E. BRUSH, Detroit: I want to thank Dr. Zininger and Dr. Priestley for their interesting comments on this subject. I did not intend to convey the impression that all islet cell tumors are functional. According to Backus, 80 per cent are silent. Multiple tumors have been found in about 15 per cent of the reported cases. The histogenesis of these tumors is very interesting, as there are alpha, beta and delta cells and a tumor may arise from any of these. The group of suspicious tumors is of great interest because they appear malignant to the pathologist and to the surgeon and yet have had a rather benign course in many instances.

DR. E. THURSTON THIEME, Ann Arbor, Mich.: Although our hospital at Ann Arbor is in the bright light of a university hospital, we are rather inclined to take up new ideas slowly, because it is a small, private hospital. Therefore, the use of sulfonamides did not begin as early or on an experimental basis, and they were not used under any planned control. We never used the large doses in the peritoneum that were so frequently used and later reported with bad effects. We did use sulfonamides in the abdomen at the start, but such use was gradually discontinued and the drugs were used intravenously. Because of the divergency of the staff, there was no plan for the intravenous use. At the present time, if a sulfonamide is used, it is used intravenously as sulfadiazine. We did not use any sulfathiazole in the abdomen, which I believe was the cause of most of the difficulty. So there was no problem as far as that is concerned. I do agree that our newer methods, as we like to consider them, in the way of postoperative care and preoperative preparation of the patients had a great deal to do with improved results. However, in trying to review the variables, as I stated before,

it seemed that one outstanding benefit was the loss of peritonitis and abdominal abscess as the cause of death and increased morbidity. It is hard to know what to attribute this to, and, as the questioner stated, it is easy to give antibiotics credit. Perhaps we are wrong. I am not sure.

DR. RUDOLF J. NOER, Detroit: Dr. Miller has asked whether the demonstration of the efficiency of the anastomoses in the wall of the intestine has altered our concept of the technic of end to end anastomosis. I might answer that simply by saying no! It has been commonly taught that not more than 2 cm. of intestine can safely be denuded of its vessels. The demonstration of these anastomoses within the intestinal wall can give us more confidence when we are forced to put up with a greater amount of vascular deprivation, but we feel that in all types of anastomosis we should like to preserve all the blood supply that can possibly be conserved.

DR. HAROLD LAUFMAN, Chicago: Aside from the operation in stages, as we have described it, the only other points in the regimen consisted in giving the animal penicillin following the second operation for just three days. After the first stage, because the bowel was left open and washed out, it was not necessary to protect the animal any further. Thereafter, the animal was treated just as any animal would be after an operation on the gastrointestinal tract.



## VARICOSITIES OF THE LESSER SAPHENOUS VEIN

WALTER W. CARROLL, M.D.

CHICAGO

THOSE varicose veins of the lower extremities which properly lend themselves to surgical correction arise largely as a result of intravenous valvular incompetency. Such relative or absolute incompetency occurs either entirely in the superficial vein or primarily in the deep and secondarily in the superficial vein. Owing to the force of gravity this anatomic defect leads to a venous reflux in the unsupported superficial veins with production of the well known stasis effects in the distal portions of the lower extremity.

Since the establishment of the concept of valvular insufficiency as a cause of varicose veins, it has been the custom to consider the phenomenon of venous reflux largely in reference to the saphenofemoral junction at the fossa ovalis. This view is due in part to the early teachings of Homans,<sup>1</sup> who pointed out the existence of the common and supposedly primary pathologic venous reflux at that point. With the passage of time, there have been a few modifications in his fundamental concept of ligation to correct the hydrostatic abnormality and thus to effect a more efficient rerouting of the venous return. The improvements have been due largely to the realization that the primary pathologic alteration is not actually located in the junctions which allow the venous backflow but is rather a matter of high valvular insufficiency in the iliac, femoral or even popliteal trunks. This insufficiency ranges from the functional inadequacy due to the demands arising from the upright position or the increased venous load from a pregnant uterus to the structural problem of complete absence of valves in some segments of vein.<sup>2</sup> Such anatomic, or rather embryologic, defects in the valvular pattern of the deep veins

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From the Department of Surgery, Northwestern University Medical School.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Homans, J.: The Operative Treatment of Varicose Veins and Ulcers, Based upon a Classification of These Lesions, *Surg., Gynec. & Obst.* **22**:143, 1916.

2. (a) McMurrich, J. P.: The Valves of the Iliac Vein, *Brit. M. J.* **2**:1699, 1906. (b) Edwards, E. A.: The Treatment of Varicose Veins, *Surg., Gynec. & Obst.* **50**:916, 1934. (c) Eger, S. A., and Casper, S. L.: Etiology of Varicose Veins from Anatomic Aspect (Absence of Valves) Based on Thirty-Eight Adult Cadavers, *J. A. M. A.* **123**:148 (Sept. 18) 1943.

lead to the production of venous hypertension, which eventually becomes manifest in the superficial veins when a junctional restraining valve becomes secondarily incompetent. This relationship can be demonstrated easily on the operating table by asking the patient to cough, thereby suddenly increasing the intravenous pressure and dilating the saphenofemoral bulb under direct vision. On the other hand, it has been directly demonstrated by anatomic dissection on cadaver material by others<sup>2c</sup> as well as by workers in the laboratory of this university.<sup>3</sup> After the local restraining valve fails to function efficiently, it is only a matter of time before varicosities develop distal to that point in the superficial venous tree.

The large cross sectional area and location of the greater saphenous bulb lends itself well to being the commonest pathway for the development of superficial varicosities. Through a proper appreciation of the existence of valvular incompetence in the iliac and high in the femoral veins, a more logical attitude has arisen concerning the complete ligation of all the tributaries of the greater saphenous vein at the point of junction with the femoral vein. Such a procedure averts needless recurrences. In addition, it has proved illogical to assume that the heavy musculature of the thigh will sufficiently compensate for this high valvular inefficiency. Experience has shown that the venous hypertension eventually may render incompetent the valves of perforating veins, allowing the reflux to reach the superficial tree at some point or other, with the production of related varicosities. This fundamental concept has served to justify a more careful search for pathologic perforating branches lower in the thigh and leg. Anatomic studies have placed the discovery of incompetent perforators on a more predictable scale, with the result that they are not only more commonly sought out but also more accurately located and surgically corrected.<sup>4</sup>

#### LESSER SAPHENOUS VEIN

In a certain sense, the lesser saphenous vein could be catalogued as a perforator, but, because it is an established and constant anatomic entity, I prefer to consider it on a plane comparable with that of the greater saphenous vein in order that it may receive its rightful emphasis. There has been surprisingly little reference in the literature to the role played by the lesser saphenous vein in the production of varicosities in the lower leg. This perhaps is in part due to the fact that in 1934 Edwards, in his excellent paper on venous valvular anatomy, dismissed

3. Anson, B. J.: Personal communication to the author.

4. (a) Linton, R. R.: The Communicating Veins of the Lower Leg and Operative Technique for Their Ligation, *Ann. Surg.* **107**:582, 1938. (b) Sherman, R. S.: Varicose Veins, *ibid.* **120**:772, 1944. (c) Massell, T. B., and Ettinger, J.: Phlebography in Varicose Veins, *ibid.* **127**:1217, 1948.

the entire problem of primary incompetency of the lesser saphenous vein as largely nonexistent. Old and even recent monographs contain reference to the idea that varicosities located in the area of the lesser saphenous distribution are the result of the well known superficial collateral anastomotic connections with the greater saphenous system. There is no doubt that this type of secondary involvement of the lesser saphenous system does occur in a fair number of persons and that its correction follows multiple ligation of the greater saphenous system and disconnection of the two systems at the point of major communication. On the other hand, a mere passing mention of the possible existence of a primary reflux in the lesser saphenous system of veins has been made by Homans,<sup>5</sup> Linton<sup>6</sup> and Sherman.<sup>4b</sup> Sarma<sup>7</sup> reported an incidence of 0.5 per cent in 1,000 patients treated by ligation. In 1942, Heyerdale<sup>8</sup> stated that he thought that too much attention was being given to a search for incompetent perforators when a reflux from the lesser saphenous veins otherwise would explain the presence of varicosities in the lower leg. Two statistical studies<sup>9</sup> were reported shortly thereafter in which some interest in the problem was indicated by inclusion of a tabulation of the incidence of incompetency of the lesser saphenous vein, shown to be 3.8 and 7 per cent, respectively. My own first report<sup>10</sup> was made in 1946, describing personal experiences with this problem. A very recent report<sup>11</sup> on 452 operations on the lower extremities made no tabular reference to any procedure directed at the lesser saphenous vein. It is interesting to note that the last-mentioned authors admit an over-all recurrence rate of 21 per cent following what appeared to be adequate simple ligation of the greater saphenous vein, ligation combined with good retrograde sclerosis or ligation combined with proper stripping and phlebectomy procedures.

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5. Homans, J.: *Circulatory Diseases of the Extremities*, New York, The Macmillan Company, 1939.

6. Linton, R. R., and Keeley, J. K.: Postphlebotic Varicose Ulcer, *Am. Heart J.* **17**:27, 1939.

7. Sarma, P. J.: Saphenous Vein Ligation, *S. Clin. North America* **18**:129, 1938.

8. Heyerdale, W. W., and Anderson, E. M.: Diagnosis and Occurrence of Communicating Veins in the Treatment of Varicose Veins, *Proc. Staff Meet., Mayo Clin.* **17**:221, 1942.

9. Pearce, M. B.: Varicose Veins: Technique for Rapid Obliteration, *Surgery* **14**:901, 1943. Larson, R. A., and Smith, F. L.: Evaluation of Observations in Four Hundred and Ninety-One Cases of Varicose Veins, *Proc. Staff Meet., Mayo Clin.* **18**:400, 1943.

10. Carroll, W. W.: Venous Surgery, *Quart. Bull. Northwestern Univ. M. School* **20**:373, 1946.

11. McElwee, R. S., Jr., and Maisel, B.: Study of the Results of Surgical Treatment of Varicose Veins, *Ann. Surg.* **126**:350, 1947.

A review of our clinical experience indicates that in addition to the accepted incompetency at the saphenofemoral junction and the usual perforators in the thigh and lower leg, we have seen a substantial number of instances of primary venous reflux in the lesser saphenous vein. To date, in 515 lower extremities consecutively operated on, there were 60 instances of this type of reflux which necessitated ligation for correction. This represents an incidence of 11.6 per cent. Of these extremities, 44 were handled by ligation of the lesser saphenous vein alone, while in 16 instances ligation of the greater saphenous vein also was carried out because either of suspicion or of the actual presence of obvious incompetency in both systems. The remaining 450 extremities presented varicosities which were thought to arise entirely from the greater saphenous system. It is worth while to point out that of the 44 extremities subjected to the procedure of ligation of the lesser saphenous vein alone, 6 already had received ligation of the greater saphenous vein elsewhere. One might feel that these should be listed under the combined procedure, but it was apparent that little benefit had accrued from the previous operation; hence they were included in the group receiving ligation of the lesser saphenous vein alone. One might conclude from this fact that attention should routinely be given to the popliteal space in order to assess correctly the role played by the lesser saphenous vein in the production of the varicosities at hand.

#### ANATOMY OF THE LESSER SAPHENOUS VEIN

The anatomic course of the lesser saphenous vein undoubtedly has been the cause of previous failure to recognize its relationship to the varicosities under consideration. This vein drains the dorsum of the foot and the posterolateral aspect of the lower leg, to empty into the popliteal vein above the flexion crease of the popliteal space. In a few persons this vein progresses cephalad in the subcutaneous tissues, penetrating the fascia at some point in the lower portion of the popliteal space to enter the popliteal vein at a sharp angle (fig. 1). Assuming such a superficial course, one would suspect that any primary venous reflux through this route would result in varicosities located high in the posterior part of the calf, showing some externally evident relationship to this system of veins. It is our experience that such a relationship would be logical when this particular anatomic pattern exists, but, on the other hand, this pattern is not common.

The crux of the matter lies in recognition of the fact that the lesser saphenous vein penetrates the fascia at variable points lower in the calf and passes upward at a deeper level, well out of sight of the casual examiner's eye, to be found only by means of careful palpation. (If one keeps in mind this concept of venous reflux as the essential factor

in the production of varicosities, this point of penetration may well be referred to as the point of emergence.) This fascial penetration (or emergence), in our experience, is at a point between one third and two thirds of the distance from the popliteal crease to the ankle joint (fig. 1 *B*). As a result there is a critical area extending over one third to two thirds of the upper posterior aspect of the calf that usually is entirely free of evident varicosities when the primary reflux is located in the lesser saphenous system. In addition, it is possible because of the free anastomosis between the two systems in the lower leg that distal medial branches may be dilated and varicose from reflux from the lesser saphenous vein. In such circumstances, it may mistakenly

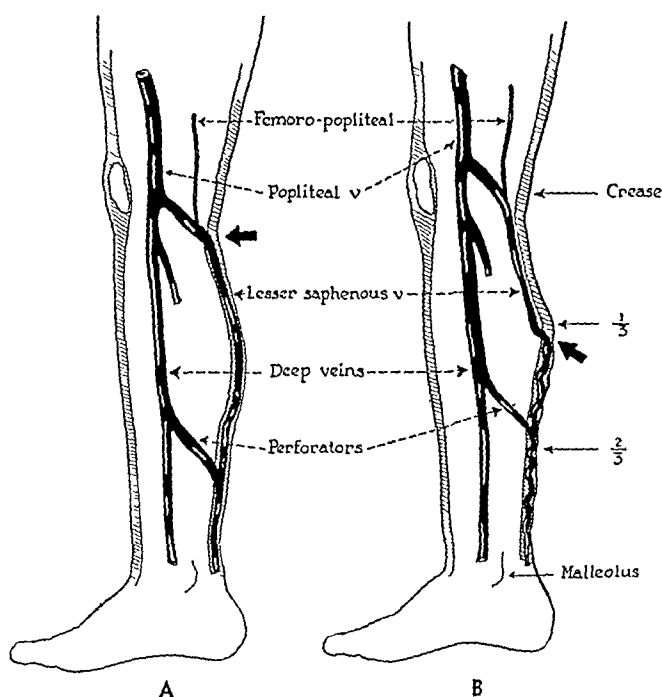


Fig. 1.—Superficial and subfascial course of the lesser saphenous vein. *A*, occasional pattern of fascial penetration; *B*, common pattern of fascial penetration.

appear that only the greater saphenous system is implicated, the lesser saphenous component being entirely overlooked. Anatomic dissections in our own laboratory as well as observations in the operating room have verified these clinical impressions, the vein occasionally being found to join the popliteal vein at a very high level.

#### METHOD OF EXAMINATION

After evaluation of the thigh has been completed, the lesser saphenous vein should be examined from the posterior aspect of the calf. With the patient standing on a high platform, it is important

first to ascertain from general inspection whether one might expect to find an incompetent lesser saphenous vein. A smooth upper calf with varicosities starting midway down and extending toward the heel and around to the lateral aspect of the ankle and dorsum of the foot should raise immediate suspicion (fig. 2). Any distal varicosities which seem to have no obvious relationship to the medial tributaries

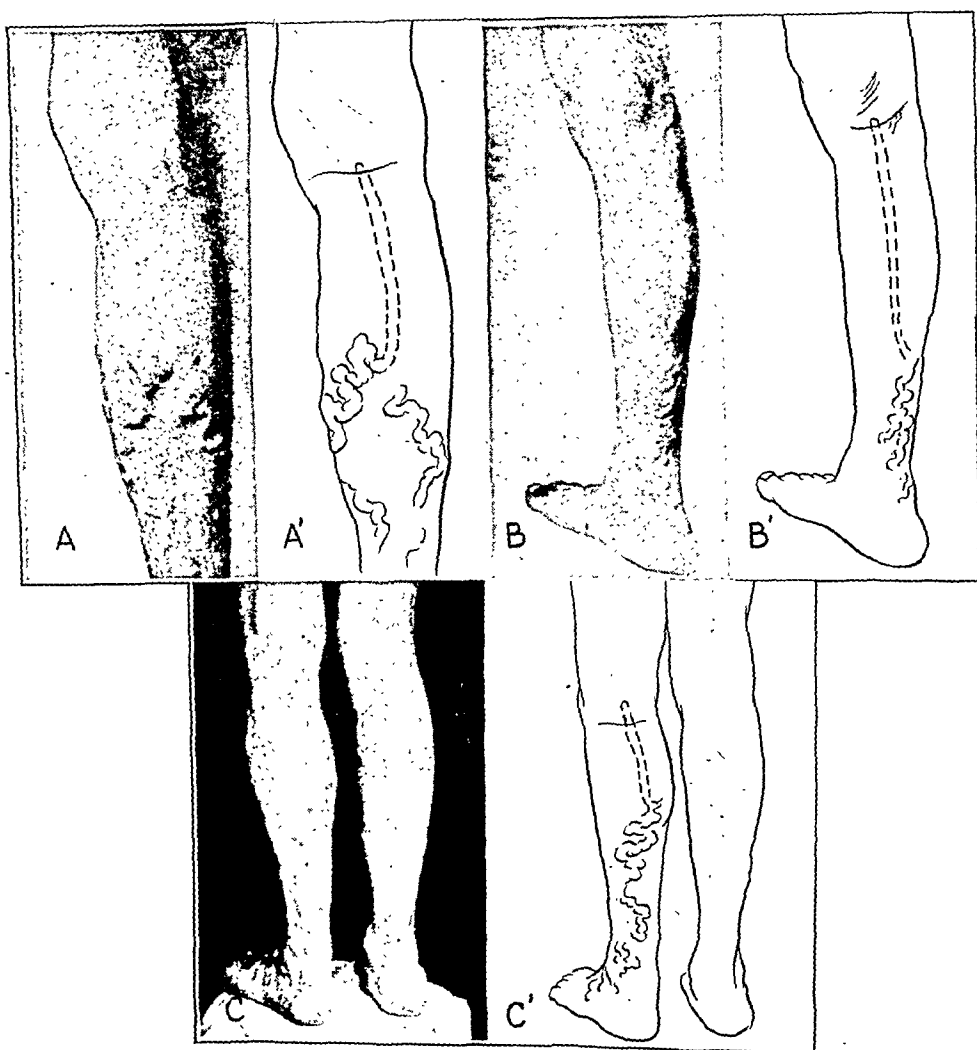
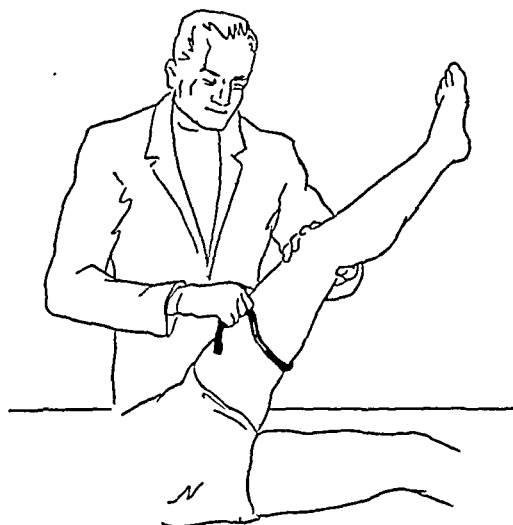


Fig. 2.—Varicosities resulting from primary venous reflux in the lesser saphenous system.

of the greater saphenous vein should be suspect. The third large group includes those which persist after previous adequate ligation of the greater saphenous vein, provided conclusive proof is present that there are no anteromedially located incompetent perforators. When the knee is slightly flexed and the weight is borne by the opposite extremity, there is sufficient relaxation of the upper calf and popliteal space for

the examiner to palpate for the vein. The normal vein cannot be palpated except in thin persons; hence if palpation at or just below the transverse crease in the skin results in the discovery of a firm venous trunk it must be considered significant. Repeated compression of the

A



B

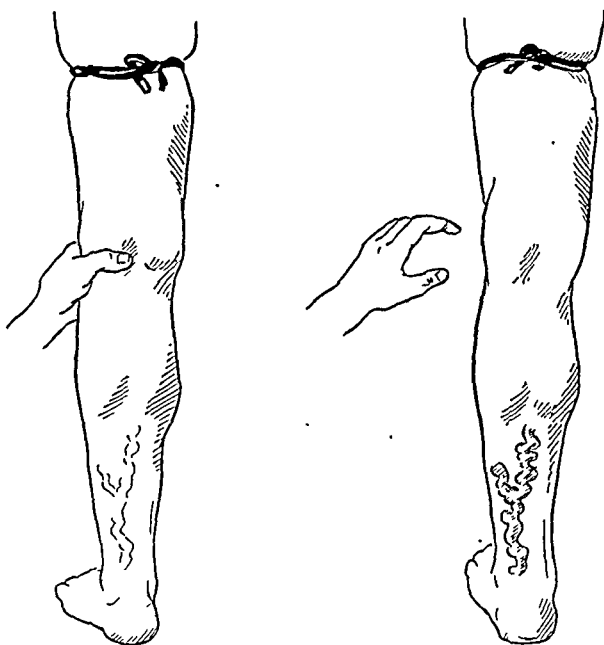


Fig. 3.—Thumb compression tourniquet test for evaluation of incompetency of the lesser saphenous system.

lower varicosities which communicate with this trunk may aid in finding the vein through the upward transmitted impulse (modified

Schwartz test). Once its discovery has placed the vein under suspicion, then the principles of the tourniquet tests can be applied.

With the proper use of soft rubber tubing constrictors, either single or multiple, the problem of detecting incompetent perforators in the thigh or calf is largely solved. In some persons this also may be sufficient for the lesser saphenous vein,<sup>12</sup> but I feel that this should not be relied on because of the fact that the vein lies well beneath the fascia and deep in the popliteal space, protected from circumferential compression by the hamstring tendons exactly at the point where the test should be most accurate. Because of this anatomic relationship, the application of the thumb is admirably suited to the purpose. The veins are emptied by elevation of the leg, and a section of soft rubber tubing is applied to the lower third of the thigh to secure control of any possible reflux through the greater saphenous system (if this is necessary). The popliteal space then is compressed with the thumb while the remaining fingers take a firm grip on the anterior aspect of the knee for stabilization of the compression (fig. 3). The patient then is allowed to stand, the thumb compression being maintained for twenty to thirty seconds. It then will be obvious that if the veins do not fill the source of the reflux has been found (fig. 3 B). This is immediately verified by removing the thumb compression and noting that the varicosities immediately fill from above downward. The tourniquet around the thigh is left in place to eliminate the possibility of any greater saphenous reflux throughout this procedure.

#### TREATMENT

The principle of ligation for correction of varicosities of the lesser saphenous vein applies exactly as it does to any perforator in the thigh or lower leg. The lesser saphenous vein lends itself well to proper ligation at the point of junction with the deep system in much the same way as does the greater saphenous vein. As in other instances, we have found it convenient to mark the longitudinal course of the subfascial trunk, even though the transverse incision across the popliteal space is used. The transverse incision is more physiologic and anatomic; it heals well and allows for adequate exposure of the vein and its branches. It must be placed about 1 to 3 cm. above the crease because the vein always enters the popliteal vein at a point higher than physical examination would suggest. In the event that the incision has been placed too low, it can be extended upward at its lateral end in the form of an "L" or merely lengthened both medially and laterally to afford sufficient retraction of the skin. The well defined fascia can be incised

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12. Steiner, C. A., and Palmer, L. H.: Simplification of Diagnosis of Varicose Veins, *Ann. Surg.* **127**:362, 1948



either transversely or longitudinally as desired (fig. 4). The tibial nerve and its posterior femoral cutaneous sensory branch should be carefully retracted to avoid injury. In addition to the main trunk joining the popliteal vein, there usually will be found at this point an upward continuation known as the femoropopliteal vein which empties either into the femoral vein at a higher level or, more commonly, into the profunda femoris vein. This must be ligated not only to prevent reflux which might develop later but also to aid in complete mobilization of the saphenopopliteal junction point for the highest possible ligation (fig. 4 *B*). An occasional connection with the greater saphenous vein also is found at this level. In the depths of the wound there occasionally is found a direct perforating branch between the lesser saphenous and

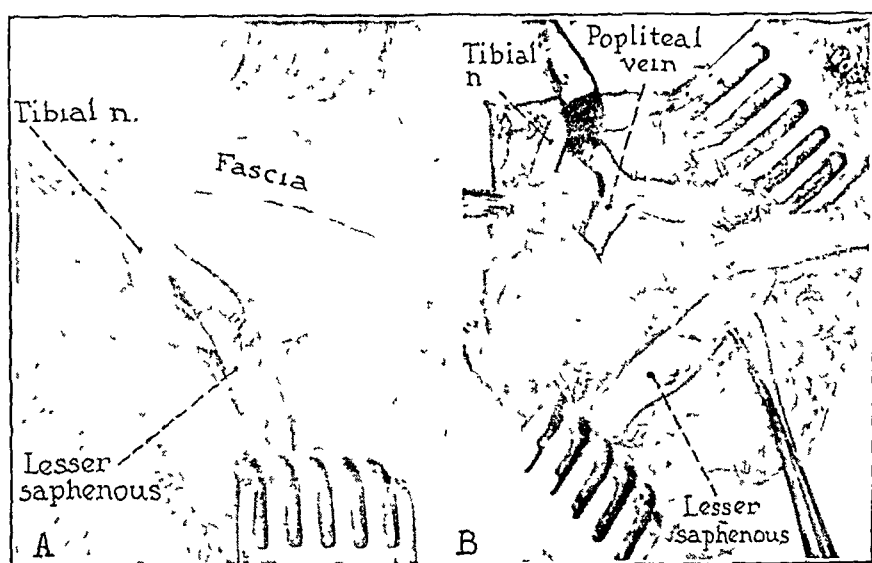


Fig. 4.—Photographs made at operation. *A*, fascia incised transversely showing close relationship of enlarged lesser saphenous vein to tibial nerve. *B*, junction of lesser saphenous and popliteal veins with tibial nerve retracted.

the deep system 1 or 2 cm. distal to the main junction. This may connect with one of the venae comites below their point of fusion to form the popliteal vein. Such a perforator also must be ligated and divided when present. In cases of doubt concerning the existence of other, more distal, perforating connections with the tibial vessels, a short longitudinal incision can be made at the point of fascial emergence. This will facilitate exploration and in some instances may allow the entire subfascial trunk to be excised if desired. Excision of the adjoining large superficial varices also is in order, whereas distal injection with sclerosing solution can be performed for small branches if desired and if not otherwise contraindicated.

Immediately after operation, the patient should be encouraged to walk as after any other venous ligation. A firm elastic roller from the toes to the lower thigh will be of help for temporary vascular support as well as to add compression to the healing wounds. The patient may wish to walk with the knee slightly flexed for the first day or two, a mechanical adjustment which certainly does not hinder good healing of the wound. Women may be requested to wear a higher-heeled shoe on the treated side to achieve this slight flexion for the sake of comfort and to prevent undue tension on the wound.

When ligation of the great saphenous vein also is planned for the same leg, I have found it expedient to postpone the procedure in the groin until another time.

#### RESULTS

Follow-up analyses of patients who have had surgical correction of varicose veins frequently fail to take into account many of the adjunctive measures necessary for a satisfactory result. The anatomic study and the procedures herein described constitute merely a small but significant part of the entire diagnostic and therapeutic program for such patients. Appreciating this fact, I do not wish to report a "success story." Suffice it to say that the results have been most gratifying. A considerable degree of alleviation of the distal venous stasis effects has been achieved, as would be expected to follow elimination of as much as possible of the pathologic venous reflux. When the location of the latter has been in doubt, we have for some time found phlebograms to be of great help, especially after the ordinary levels have been surgically explored. There is no one operation which will solve the problems of all these patients, but thorough unbiased evaluation of each extremity may result in fewer therapeutic failures.

#### SUMMARY

In 515 extremities presenting varicose veins secondary to valvular insufficiency, there were 60 instances of primary venous reflux in the lesser saphenous system.

Ligation of the lesser saphenous vein and its tributaries at the popliteal junction corrects this pathologic reflux and effects a more efficient rerouting of venous return.

A clinical test is described which has been of value in localizing this reflux through the saphenopopliteal junction.

## SUBSTITUTION OF THE URINARY BLADDER WITH AN ISOLATED SEGMENT OF SIGMOID COLON

J. DEWEY BISGARD, M.D.

AND

H. HARPER KERR, M.D.

OMAHA

THE PRESERVATION or restitution of normal function, although not always essential, is certainly the most desirable goal to be attained after any surgical procedure. In this respect, all operations for total removal of the urinary bladder fail. This does not imply that the present modifications of the Coffey operation<sup>1</sup> are not satisfactory, for there is much evidence to the contrary, but it does imply, rather, that these operations do not attain the ideal of restoring the normal route of urinary excretion.

Assuming that it was possible to preserve bladder function and to use an isolated segment of sigmoid colon as a substitute bladder, we planned a two stage operation and carried it through to completion in 5 of the 7 dogs in which it was attempted. There were 4 females and 1 male. The results obtained in the first 2 animals were reported in 1943.

The technic of the operation, previously reported,<sup>2</sup> is outlined in the drawings in figure 1.

. . . It was performed in two stages. At the first stage the right ureter was divided at its junction with the bladder and dissected from its bed sufficiently to allow its transplantation to a loop of the sigmoid which had been selected to replace the bladder. The most proximal portion of the sigmoid which could be carried down to the position of the bladder without tension was selected. The ureter was transplanted by means of a strangulation suture at the head of a 1.5

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Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. Coffey, R. C.: Production of Aseptic Uretero-Enterostomy by a Suture Transfixing Ureteral Wall and Intestinal Mucosa, *J. A. M. A.*, **94**:1748 (May 31) 1930; Transplantation of Ureters into Large Intestine by Submucous Implantation, *ibid.* **99**:1320 (Oct. 15) 1932; Further Studies and Experiences with Transfixion Suture Technic (Technic No. 3) for Transplantation of the Ureters into Large Intestine, *Northwest. Med.* **32**:31 (Jan.) 1933.

2. Bisgard, J. D.: Substitution of the Urinary Bladder with a Segment of Sigmoid, *Ann. Surg.* **117**:106-109 (Jan.) 1943.

cm. submucosal bed, as described by Coffey in his revised aseptic technic. Four or five centimeters above this point, the sigmoid was divided between clamps with a cautery. The distal end was closed aseptically with two rows of sutures and dropped into the pelvis. The proximal end was brought out through the wound as a temporary colostomy. The abdominal wall was closed around the exteriorized proximal end, the clamp removed, and the free edge of the bowel sutured to the skin around its circumference. Within three or four days liquid stools were passed by rectum. On the 10th postoperative day, and for four days subsequently, the blind pouch of rectum and distal sigmoid was irrigated with salt solution

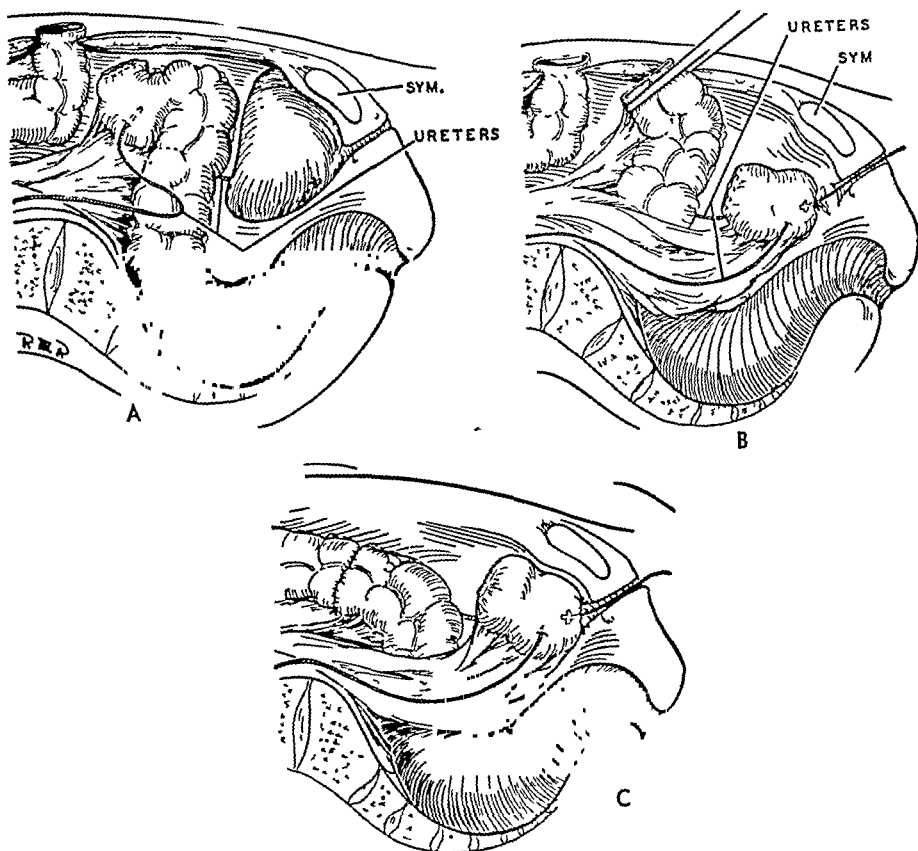


Fig. 1.—At the first stage (*A*) the right ureter is transplanted to the segment of the sigmoid colon which will subsequently be utilized as a substitute bladder. The bowel is divided above this point, the distal end infolded and the proximal end exteriorized as a colostomy. *B* and *C* show the steps of the second stage; *C* the completed bladder, transplantation of the left ureter, isolation of the sigmoid bladder and suture of its distal free end to the urethra and reestablishment of continuity of the colon. (Reprinted with permission of J. B. Lippincott Company from Bisgard, J. D.: Substitution of the Urinary Bladder with a Segment of Sigmoid, *Ann. Surg.* **117**:106 (Jan.) 1943.

until the solution returned clear [in an endeavor to render it relatively sterile for the second operation].

On [or soon after] the 14th day the second stage was performed. This consisted of the following steps: The left ureter was divided at its junction with the bladder dissected from its bed and laid aside. The bladder was then resected

and a small mushroom catheter threaded through the urethra from within out, with the mushroom-end remaining in the peritoneal cavity. The distal sigmoid was divided about 4 to 6 cm. distal to the site of previous ureteral implantation. The mushroom tip of the catheter was inserted into this isolated segment of sigmoid and secured within the lumen with a purse string suture placed around it about 1 cm. above the free edge. With traction applied to the catheter beyond the meatus by an assistant, the open end of the isolated pouch of sigmoid was drawn down to the cut end of the urethra and the two edges approximated with interrupted mattress sutures. The left ureter was then placed in a submucosal bed and implanted directly into the lumen of the pouch. [In all but 2 animals] the colostomized, or proximal end of the sigmoid was dissected free from the abdominal wall and the continuity of the bowel reestablished by an end to end anastomosis between it and the free end of the distal sigmoid.<sup>2</sup>

In 2 animals the bowel was not anastomosed, but, rather, the proximal end was left exteriorized as a permanent colostomy for studies of motor function. After the abdomen was closed, the catheter was cut off at the urethral meatus and fixed to the meatus with a suture. Five days later it was removed.

By dividing the operation into two stages, two important objectives were accomplished. Continuous urinary excretory function was assured. The success of the first ureteral transplant was established before disturbing the other ureter, thus avoiding the hazard of anuria. By diverting the fecal current through the temporary colostomy, and as a result of irrigations, the distal pouch was rendered relatively aseptic. This made it possible to isolate the segment of sigmoid and to carry through the rest of the operation with but slight risk of peritonitis.<sup>2</sup>

All 5 dogs remained well and appeared to be normal until they were killed to obtain specimens. Two were killed at four months after operation, 1 at one year and 2 at two years.

## RESULTS

The results of the experiments may be summarized briefly as follows.

*Continence.*—In all animals urinary continence developed within a day or two after the removal of the urethral catheter. Periodically throughout the life of the animals catheterizations were done, and never was there more than 2 ounces (60 cc.) of urine recovered. Often the bladder contained less than  $\frac{1}{2}$  ounce (15 cm.). Before the catheter was removed, 2 ounces of water was instilled and in every instance it was retained for fifteen minutes or longer.

In 2 dogs the quantity and frequency of urination was measured. This was accomplished with the animals in drainage cages, all urine draining from the floor of the cage into a receptacle equipped with a float with a writing arm which inscribed a quantitative record on a smoked drum. One of these records appears in figure 2. In both animals urination occurred at intervals of fifteen to forty minutes and in quantities varying from 15 to 35 cc.

*Voluntary Urination.*—The extent of voluntary control of the substitute bladder could not be definitely determined. The females squatted to urinate, but the male was usually unable to expel urine when he made the usual gesture toward trees and posts.

The motor activity of the sigmoid bladder was investigated in 2 animals by means of indwelling inflated balloons connected to a manometer which inscribed a kymographic record of the peristaltic activity. One of the records is reproduced in figure 3. It is apparent that the rhythmic contractions and the segmental peristaltic waves normally

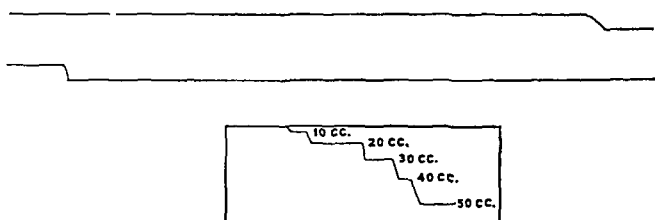


Fig. 2.—A kymographic recording of urinary output during an interval of eighty minutes. During this period the dog urinated approximately 25 cc. on two occasions.

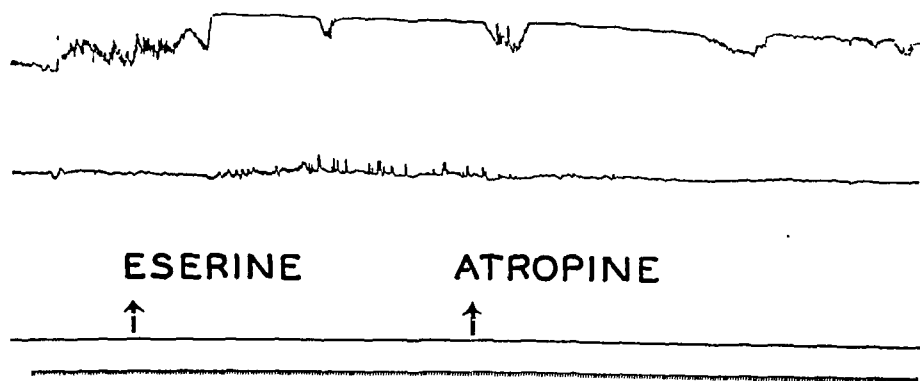


Fig. 3.—Simultaneous kymographic tracing of the motor activity of the isolated segment of sigmoid used to replace the bladder (upper one) and of the colostomized descending colon (lower). The records were obtained by means of indwelling inflated balloons. Note that in both tracings eserine produced a tonic motor response and atropine, mild inhibition; also note the preliminary record of normal rhythmic and segmental contractions.

observed in the colon remained unaltered despite the change of function. Eserine increased tonicity to the point of spasm, a much more vigorous response than that registered simultaneously by a balloon passed into the colon through the colostomy. Atropine in both segments produced the usual antagonistic (inhibitory) response.

*Urinary Infection.*—At no time was there subjective evidence of infection of the urinary tract in any of the animals. However, no bacteriologic studies were done. In repeated examinations of the urine at varied intervals after one month following operation there were no abnormalities discerned. The centrifuged sediment invariably contained a few pus cells, but there was never gross pyuria. Furthermore, there was no evidence at postmortem examination that an infection of the urinary tract existed or had ever existed. In all 5 animals the kidneys, ureters and sigmoid bladder were normal in appearance. There was no dilatation of the ureters and of the pelvis of the kidneys. Microscopic examination of the segment of sigmoid showed a normal colon



Fig. 4.—Postmortem specimen. The kidneys and ureters are normal. In the open sigmoid bladder and urethra note line of union, also, probes in the ureteral orifices. (Reprinted with permission of J. B. Lippincott Company from Bisgard, J. D.: Substitution of the Urinary Bladder with a Segment of Sigmoid, *Ann. Surg.* **117**:106 (Jan.) 1943.

histologic picture. It had not been altered with a change of function even after two years.

#### SUMMARY

A two stage operation for resection of the bladder and for its replacement with an isolated segment of sigmoid colon is presented. The operation was performed successfully in 5 dogs, and in each instance the substitute bladder functioned satisfactorily. In no instance was there evidence of infection of the urinary tract.

## CONCLUSION

The success of this operation in animals raises the question of its applicability to problems encountered in man. First, it is a much more formidable procedure than the Coffey type of operation, and it is very doubtful that the possible advantages that it might give would compensate the increased operative risk except for benign lesions necessitating total removal of the bladder. In extrophy, practically the only lesion of this type, the open exteriorized urethra makes the operation impossible.

In malignant disease adequate resection often includes a portion of the urethra (including the prostate gland in the male) and with it the prospect of loss of continence.



## REDUCTION IN MORTALITY AND LOSS OF LIMBS IN DIABETIC GANGRENE AND INFECTION

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AND

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IN 1939 a study was made of the amputations done for diabetic gangrene and infection at the Buffalo General Hospital during the preceding seven years. The mortality for all cases was 35 per cent and for major amputations, 41 per cent. A review of the literature showed that these were not comparatively high figures, although a few centers were beginning to report reduction in mortality through methods aimed at quick riddance of infection. There had been no significant reduction in the mortality in this hospital during the seven years covered by the study. Analysis disclosed that in 75 per cent of all our cases there was some infection of the stump or amputation site. In all the fatal cases postoperative infection had been present.

It seemed, then, that postoperative infection played the major role in maintaining the high mortality rate. The factors of age, blood supply and severity of diabetes appeared much less important, though, of course, it was recognized that adequate medical management in cooperation with surgical treatment was essential. In order to reduce the incidence of infection, during the next few years a two stage amputation was done in cases of severe infections necessitating major amputations. The first stage consisted of a guillotine amputation through the mid-calf to eliminate all infected tissue; no attempt at closure was made at this time. A definitive supracondylar amputation was done later when the guillotine stump was clean and the patient's general condition had improved. In a number of these cases cultures taken from the apparently healthy muscle at the time of the guillotine amputation yielded the same organisms as were cultured from the infected foot. However, only 1 of a series of 28 patients so treated had any evidence of infection in the stump of the definitive thigh amputation, and that

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was a minor infection. There was only 1 death, too, in this series and at autopsy the patient was shown to have a massive pulmonary embolism from a mural thrombus in the heart. This was a remarkable reduction in mortality and incidence of postoperative infection. The mortality for all cases during the five year period 1940 to 1944, inclusive, was 8.8 per cent, and that for cases in which guillotine amputation had been done was 3.5 per cent (table 1). The use of sulfonamide drugs

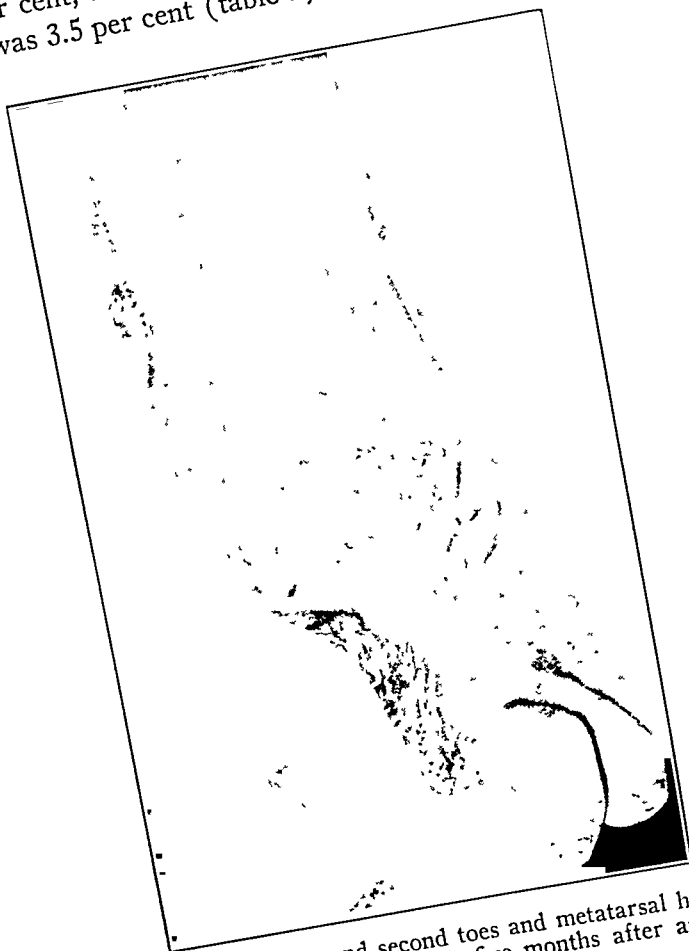


Fig. 1.—Amputation of first and second toes and metatarsal heads for gangrene. Skin graft completely healed. Photograph five months after amputation.

TABLE 1.—Comparative Mortality by Periods

Period	Cases, Number	Deaths, Number	Mortality, Percentage
1933-1939.....	140	49	35
1940-1944.....	136	12	8.8
Guillotine.....	28	1	..
1945-1945.....	122	5	4.1

during this period was an additional factor, though they were not used routinely, especially during the early part of the period.

In 1943 some badly infected feet were treated by local amputation and débridement of all infected tissue, as had been described earlier by Zierold,<sup>1</sup> rather than by guillotine amputation. Often the amputation site so treated became covered with such healthy-looking granulations that it was decided to cover some of them with skin grafts. Early in 1945 penicillin began to come into general use, and, with its use, it became safer to do local amputations, with less fear of danger from spreading infection. From this time on the procedure of local amputation and débridement was carried out in steadily increasing numbers of cases, with less and less regard to the status of the local blood supply. At the present time most of our major amputations are done



Fig 2—Wedge amputation of second, third and fourth toes done for severe spreading infection and cellulitis of foot. Photograph four weeks after grafting

in cases in which a local amputation has failed to heal because of poor blood supply. As would be expected, the most favorable cases for local amputation are those that still have a comparatively good blood supply. Yet feet with apparently very poor blood supply often heal remarkably well, and a few of our best results are in patients who had local amputations only because they refused a major amputation.

1 Zierold, A A Gangrene of Extremity in the Diabetic, *Ann. Surg.* **110**:723-730 (Oct) 1939

As shown in tables 2 and 3, during the four year period 1945 to 1948 70 per cent of all amputations in diabetic patients were local amputations and only 30 per cent were amputations through the leg or thigh. During the period 1933 to 1939 these figures had been reversed, 71 per cent of all the amputations being through the thigh and 29 per cent local. During the past four years 86 per cent of our amputations of toes and local amputations have been successful. By that we mean that they have ended in healing or the stumps have taken skin grafts successfully and a subsequent major amputation has not been required. It is readily apparent from these figures that we are now saving a large number of limbs which would formerly have been lost through major amputations.

TABLE 2.—*Distribution of Amputations by Period and by Type*

Period	Type of Amputation			
	Toe, Percentage	Leg, Percentage	Gullotine and Thigh, Percentage	Thigh, Percentage
1933-1939.....	29	...	..	71
1940-1944.....	50	4.4	21	25
1945-1948.....	70	4.9	6.5	18

TABLE 3.—*Results in Local Amputations\**

Period	Cases, Number	Successful Results, Percentage
1933-1939.....	41	46
1940-1944.....	68	63
1945-1948.....	86	86

\* Amputations of toes and of part of the foot.

The successful treatment of the diabetic patient with gangrene or infection of the extremities depends on a number of factors, high among which stands close cooperation between the surgeon and the internist. Without the best possible medical management of the diabetes and its complications relatively little can be accomplished by operation alone. In many of our cases with gangrene and impending or actual coma, strenuous treatment by the internist has brought the situation sufficiently under control to allow surgical intervention within a few hours following the patient's admission to the hospital.

Our present procedure consists in (1) close cooperation between internist and the surgeon in caring for the patient as well as for his gangrene, (2) use of large doses of penicillin and other antibiotics as indicated to bring infection under control and (3) early and complete local amputation and débridement of gangrenous infected tissue. The type of operation is selected to allow no barrier to remain at

the amputation site which might cause the collection, or interfere with the drainage, of pus and infected exudate. Amputations of toes and parts of the foot are either true guillotine procedures or of the "wedging" or guttering type, the surfaces being so arranged as always to allow complete dependent drainage with the patient in bed. Wet dressings are used only in case of good blood supply. In cases in which the blood supply is poor, bland ointment dressings are used and the entire extremity kept wrapped in thick layers of cotton bathing and flannel bandage. When the area shows healthy granulations



Fig. 3—Amputation of second toe and metatarsal head for osteomyelitis and perforating sinus. Photograph two weeks after application of pinch grafts

on the surface, it is covered with small pinch grafts taken from the same or the opposite thigh. Pinch grafts are used because of their ability to take almost universally in spite of adverse conditions. In our hands, they have given well covered, satisfactory surfaces. Care must be taken not to apply too much pressure in dressings covering the grafts and to avoid pressure on other parts of the foot, especially in case of badly compromised circulation.

The kind of foot that the patient has left after this procedure depends on the extent of local amputation and débridement necessary.

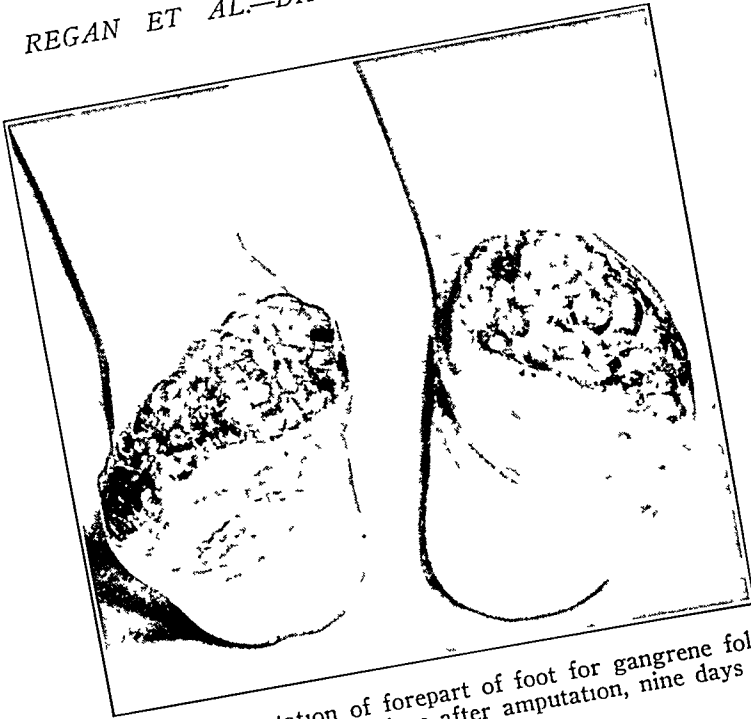


Fig. 4—Bilateral amputation of forepart of foot for gangrene following exposure to cold. Photograph nineteen days after amputation, nine days after application of grafts

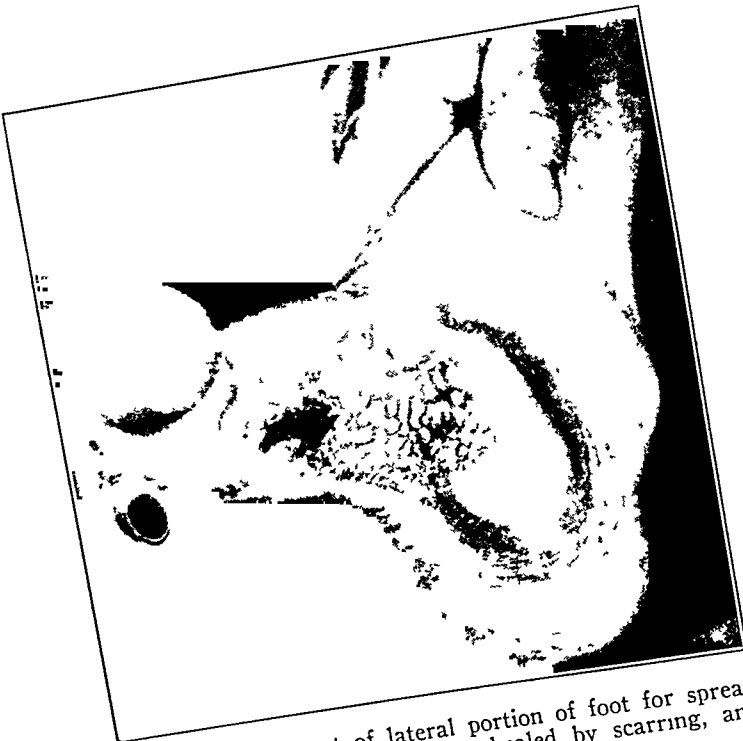


Fig 5—Amputation of most of lateral portion of foot for spreading infection with deep slough. Much of the area has healed by scarring, and the rest is covered with pinch grafts

After single or multiple amputations of toes without extension into the metatarsal area, they are almost always good walking feet. After the more extensive amputations something is often left to be desired, by orthopedic standards. In many of our cases there has not yet been sufficient time for follow-up study, but in those that have the results have been encouraging. Even poor-looking feet often make good weight-bearing stumps. There is a tremendous difference in the patient's psychologic reaction to a local and to a major amputation. Finally, since most diabetic patients who have a major amputation never learn to use a prosthesis satisfactorily, saving a limb often saves the patient from complete invalidism.

#### SUMMARY

A survey of amputations for diabetic gangrene and infection at the Buffalo General Hospital from 1933 through 1948 is presented.

Mortality has been reduced from 35 per cent to 4.1 per cent.

The present procedure for local amputation is described. Local amputations now comprise 70 per cent of the total number, whereas amputations through the thigh formerly were 71 per cent of total.

In 86 per cent of local amputations there has been successful healing.

A large number of extremities are now being saved which would formerly have been lost through major amputations.

# PROMPT POSTOPERATIVE ACTIVITY AFTER HERNIOPLASTY

Its Influence on Incidence of Complications and Rate of Recurrence

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COOPERSTOWN, N. Y.

MANY POSTOPERATIVE complications are favorably affected by prompt ambulation and other accelerated modifications in traditional convalescent care. On the contrary, the incidence of thrombosis in the deep veins of the lower extremities and of pulmonary infarction due to small, nonfatal emboli is unaltered.

Wounds heal kindly, and the rate of recurrence following hernioplasties of all types is significantly less among promptly ambulatory patients than among those who remain inactive in bed for ten to fourteen days after operation.

The data herewith submitted are offered in support of these assertions.

## CLINICAL MATERIAL

The study is based on a critical survey of all the cases in which hernioplasty was performed at the Mary Imogene Bassett Hospital during the sixteen years from 1933 through 1948. These include cases of inguinal, femoral, epigastric, umbilical and ventral hernias, various combinations of these with inguinal ruptures, diaphragmatic and internal hernias and 2 cases of abscesses in inguinal sacs; a total of 467 operations was done (table 1).

These have been grouped according to the rapidity of postoperative mobilization of the patients. "Prompt" activity connotes arising from bed and walking within twenty-four hours after operation, occasionally during the afternoon or evening of the same day, never from the table to bed as advocated by some surgeons; "early" refers to ambulation commencing on the second, third or fourth day; "late" applies to mobilization which is not undertaken until the fifth day or after, usually on the tenth or twelfth postoperative day. No attempt has been made to grade the activity of "children"; this category includes all those from birth through 12 years of age.

There has been no selection of patients for specific plans of postoperative activity. Early ambulation was instituted in this hospital in 1940. The patients on whom hernioplasty was performed prior to that year remained in bed for traditional periods of convalescence, depending on the age of the patient and the type of hernia. During 1940 recumbency of two, three or four days only was allowed. Since 1941 all patients have been mobilized within twenty-four hours after hernioplasty, except for a very few in whom there were obvious and definite contraindications. These include acute postoperative coronary thrombosis, cerebral

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thrombosis or hemorrhage with paralysis of the lower extremities and peritonitis of bacterial origin secondary to perforation of the intestine by strangulation.

Three hundred forty-six hernias in this survey were unassociated with pre-operative complications (table 2). The mortality in this group was 0.6 per cent.

TABLE 1.—*Tabulation of the Types of Hernioplastics in This Study*

Hernioplastics	Patients						Total
	Adults				None; Post-operative Death	Children	
	Ambulation						
	Prompt	Early	Late				
Unilateral inguinal.....	161	12	97	5	53	328	
Bilateral inguinal.....	27	0	5	1	5	38	
Unilateral femoral.....	12	6	15	3	0	36	
Umbilical.....	5	1	6	0	13	25	
Epigastric.....	1	0	6	0	0	7	
Postoperative ventral.....	7	2	9	1	0	19	
Post-traumatic ventral.....	0	0	1	0	0	1	
Inguinal and umbilical.....	1	0	0	0	0	1	
Inguinal and postoperative ventral....	1	0	1	0	0	2	
Inguinal and unilateral femoral.....	1	0	2	1	0	4	
Inguinal and bilateral femoral.....	0	1	0	0	0	1	
Diaphragmatic.....	1	0	1	0	0	2	
Internal.....	0	0	1	0	0	1	
Abscess in inguinal sac.....	0	0	0	2	0	2	
Total.....	217	22	144	13	71	467	

TABLE 2.—*Associated Preoperative Complications*

Complications	Patients					
	Adults					Total
	Ambulation				None; Post-operative Death	
	Prompt	Early	Late			
None.....	175	13	98	2	58	346
Incarceration of omentum.....	7	0	12	0	1	20
Incarceration of intestine or colon.....	6	0	5	0	4	15
Incarceration of omentum and intestine or colon .....	3	0	2	0	0	5
Incarceration of intestine with obstruction...	8	0	7	3	1	19
Incarceration of acutely inflamed appendix...	1	2	0	0	0	3
Incarceration of tube and ovary.....	0	0	0	0	1	1
Incarceration, organ not stated.....	0	0	0	0	2	2
Strangulation of omentum.....	3	1	4	0	0	8
Strangulation of intestine with obstruction..	12	5	14	5	4	40
Strangulation of omentum and intestine with obstruction .....	1	1	2	1	0	5
Strangulation of appendix epiploica.....	1	0	0	0	0	1
Abscess due to Escherichia coli in hernial sac..	0	0	0	2	0	2
Total .....	217	22	144	13	71	467

Death in 1 case was due to massive pulmonary embolism, and in the other to peritonitis resulting from perforation of the sigmoid by a needle and suture in the repair of a sliding hernia. One hundred and twenty-one, or 26 per cent, were associated with incarceration or strangulation of some organ or viscus and fre-

quently further complicated by intestinal obstruction (table 2). Operation was considered urgent in these cases and performed as an emergency. Eleven of the 13 deaths occurred in this group, a mortality of 9.1 per cent. The average age of the patients who died was 60.3 years.

TABLE 3.—*Postoperative Complications*

Complications	Number				
	Adults			Children	Total
	Postoperative Activity				
	Prompt	Early	Late		
Local					
Hematoma in wound, cord or scrotum *	21	1	6	3	31
Seroma in wound.....	2	0	1	0	3
Infection of wound.....	3	0	5	3	11
Cellulitis of abdominal wall ..	0	0	1	0	1
Discharge of nonabsorbable sutures ..	1	0	1	0	2
Stitch abscess ..	2	1	3	2	8
Disruption of wound (laparotomy) ..	0	0	1	0	1
Total ..	29	2	18	8	57
Cerebral					
Cerebral thrombosis with hemiplegia.....	0	0	1	0	1
Cerebral hemorrhage, suspected.....	0	0	1	0	1
Total ..	0	0	2	0	2
Cardiac *					
Anginal attacks ..	0	0	1	0	1
Coronary thrombosis, with infarction of myocardium ..	0	0	2	0	2
Decompensation with pulmonary edema and congestion ..	0	0	2	0	2
Total ..	0	0	5	0	5
Pulmonary					
Bronchitis ..	8	0	9	0	17
Bronchopneumonia * ..	4	2	12	1	19
Partial atelectasis * ..	8	0	5	0	13
Massive atelectasis * ..	0	0	2	0	2
Infarct of lung, demonstrable or suspected ..	8	1	7	0	16
Pulmonary embolism, actual or suspected * ..	0	0	5	0	5
Pleurisy ..	1	0	4	0	5
Cough, unexplained ..	4	1	4	0	9
Total ..	33	4	48	1	86
Vascular					
Thrombophlebitis, superficial or deep ..	1	0	2	0	3
Thrombosis of deep veins of legs ..	15	1	9	0	25
Thrombosis of intrinsic vessels of ..	0	0	1	0	1
Embolism of femoral artery.....	1	0	0	0	1
Total ..	17	1	12	0	30
Gastrointestinal					
Persistent hiccup ..	2	0	3	0	5
Dilatation of stomach*.....	1	0	6	0	7
Persistent abdominal distention * ..	5	0	16	0	21
Total ..	8	0	25	0	33
Genitourinary					
Postoperative inhibition of bladder					
Necessitating 1 catheterization only*....	15	3	4	0	22
Necessitating 2 or more catheterizations * ..	9	5	27	0	41
Cystitis ..	2	4	5	0	11
Total ..	26	12	36	0	74
General					
Fever of unknown origin* ..	2	0	7	4	13
Total complications ..	115	19	153	13	300
Total operations ..	217	22	157	71	467
Incidence of complications (percentage).....	53%	86%	98%	18%	64%

\* Complications of some significance, discussed in the text.

#### POSTOPERATIVE COMPLICATIONS

All the patients have been under my personal care, supervision or observation. All the hospital charts and records have been carefully reviewed and special attention paid to symptoms and signs which

suggest or indicate complications during convalescence. The number of patients who were first mobilized on the second, third or fourth day ("early") is too small to be of statistical significance, and complications in children, who are never quiet during convalescence, are too infrequent to justify consideration. Consequently, this survey is limited to a comparative study of the complications which occurred among the adult patients who were activated within the first twenty-four hours ("prompt") and those who remained in bed for an average period of 10.8 days after operation ("late"). The two groups are fairly comparable in size, 217 operations in the first and 157 in the latter (table 3).

All complications have been classified according to the system involved and are recorded in table 3. The incidence of many is unaffected favorably or adversely, by the rapidity of mobilization of the patient during convalescence. Others are very definitely influenced by prompt activation. The complications of significance are designated by an asterisk in the tabulation and discussed in some detail in succeeding paragraphs.

*Local Complications.*—Hematoma in the wound, cord or scrotum was three and one-half times as common among the patients who were out of bed and walking within twenty-four hours as among the others. All wounds were dry when closed; hence it seems probable that prompt ambulation is conducive to postoperative oozing from tiny vessels which were not bleeding during the operation. Unusually careful hemostasis is imperative when such activity is permitted.

*Cardiac Complications.*—It may or may not be important that all the cardiac complications developed among the patients who remained quiescent in bed for ten to fourteen days after operation. Many who were equally poor as operative risks were permitted to get up on the first day, walk a few steps and sit in a chair with their legs elevated without mishap.

*Pulmonary Complications.*—Bronchopneumonia occurred only one third as often among the patients who were out of bed and walking within twenty-four hours. It is unlikely that this lowered incidence of pulmonary infection was due to modern chemotherapeutic agents and antibiotics, for these drugs were not used prophylactically. Massive atelectasis was not observed among the promptly ambulatory patients. The frequency of clinically recognizable partial atelectasis was unaffected. The incidence of pulmonary infarction due to small emboli, either demonstrable or suspected, was not influenced by prompt mobilization. However, massive pulmonary embolism of sufficient magnitude to cause a fatal catastrophe did not occur among the patients who were allowed to get up on the first postoperative day and increase their activity rapidly thereafter.

*Vascular Complications.*—Thrombosis in the deep veins of the legs was not prevented, nor was the incidence of this complication lowered by prompt postoperative mobilization. In these two groups thrombosis was actually commoner among the ambulatory patients. After studying the incidence of thromboembolism among 1,519 major surgical patients operated on at the Bassett Hospital and reported in 1947<sup>1</sup>, I concluded: "Exercises in bed, ambulation within the first twenty-four hours . . . and a generally accelerated convalescence permit an early return to customary activity. Unfortunately they do not favorably influence the incidence of postoperative thrombosis nor eradicate the hazard of pulmonary embolism." The present study of the incidence of postoperative thrombosis and nonfatal embolism after hernioplasty offers additional support to the same conclusions. This opinion is contrary to that held by many authors.

*Gastrointestinal Complications.*—Postoperative dilatation of the stomach and persistent abdominal distention were very much less common after hernioplasty when patients were permitted ambulation within the first twenty-four hours and prompt resumption of a normal diet. These complications occurred only six times among the 217 ambulatory patients but twenty-two times among the 157 patients in the late group.

*Genitourinary Complications.*—The total number of patients in the two groups who required catheterization once because of postoperative inhibition of the bladder was not significantly different. However, the necessity for repeated catheterizations was much less frequent after patients were up and about on their feet.

*Fever of Unknown Origin.*—Such fever was commoner among the patients who were recumbent during convalescence. The reason is not apparent.

*Total Complications.*—The incidence of total complications among the patients who were permitted prompt ambulation was 53 per cent, 1 complication after every other operation; among those who remained in bed for an average of eleven days the incidence was 98 per cent, 1 complication after every operation. The favorable influence of prompt ambulation on the incidence of total postoperative complications is obvious.

#### RECURRENCE AFTER HERNIOPLASTY

In studying recurrence after hernioplasty it is important to allow a follow-up interval of at least one year.<sup>2</sup> Consequently, all the hernias repaired in 1948 have been excluded from this phase of the survey.

1. Powers, J. H.: Postoperative Thromboembolism, *Am. J. Med.* 3:224-230, 1947.

2. Glenn, F.: The Surgical Treatment of Five Hundred Herniae, *Ann. Surg.* 104:1024-1029, 1936.

During the fifteen years from 1933 through 1947, there were 444 hernioplasties performed on 391 patients (table 4). Prompt postoperative activity was permitted after 193 of these procedures, early activity after 19 and late ambulation after 166; the remaining 66 hernioplasties were in children.

Fifteen hernias in the late group were immediately eliminated from further study by the death of 13 patients in the hospital. There were no recurrences among the 19 patients in the early group, nor were there any among the children. However, these two groups have been discarded because the former is too small to be of statistical importance and recurrence in infancy and childhood is exceedingly rare. Also eliminated because of death after discharge from the hospital without examination at least one year later or failure to trace for

TABLE 4.—*Rate of Recurrence Following Hernioplasty*

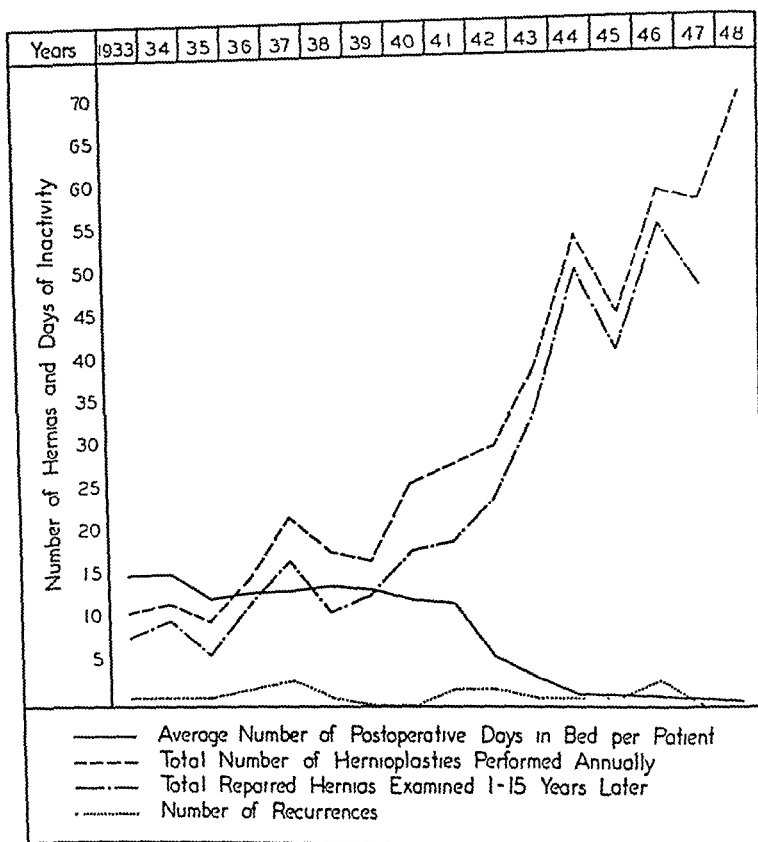
Analysis 1933-1947 Inclusive	Hernias Repaired				
	Adults Postoperative Activity			Children	Total
	Prompt	Early	Late		
Number of hernias repaired.....	193	19	166	66	444
Eliminated from further study by postoperative death of patient .....	0	0	15	0	15
Lost by death after discharge without follow-up exami- nation .....	2	..	6	..	..
Discarded because of failure to trace for at least 1 year .....	11	..	16	..	..
Adequately followed for 1 to 15 years.....	180	11	129	47	367
Duration of follow-up period.....	1-8 yr.	..	1-15 yr.	..	..
Known recurrences .....	6	0	13*	0	19
Percentage of hernias adequately followed.....	3.3	..	10.1	..	5.1

\* Only 2 of these recurred between eight and fifteen years after operation.

the same length of time were 13 hernioplasties among the promptly ambulatory patients and 22 among those in the late group. Finally remaining, adequately followed, reexamined and available for evaluation of the influence of prompt postoperative activity on the rate of recurrence were a total of 309 hernioplasties, 180 performed on patients who were promptly ambulatory after operation to be compared with 129 hernioplasties on patients whose mobilization was delayed for eleven days (table 4).

Prompt postoperative ambulation was instituted in 1941. Consequently, it was possible to reexamine the operative wounds in this group one to eight years after operation. The patients in the late group were followed for one to fifteen years. Six recurrences were discovered among the former and 13 among the latter, thereby establishing an absolute known rate of recurrence of 3.3 per cent among the patients who were allowed to get up and walk within twenty-four hours after operation and 10.1 per cent among those who remained recumbent in bed for eleven days. The known rate of recurrence for the entire group of 367 adequately followed hernias was 5.1 per cent.

The correlation of postoperative activity with rate of recurrence after hernioplasty is expressed graphically in the chart. In spite of the tremendous increase in the number of hernias operated on annually at the Mary Imogene Bassett Hospital during the past fifteen years and the striking decrease in the average length of time spent in bed by each patient after operation, the number of recurrences has remained essentially unchanged over the years. The annual rate of known recurrence has fallen steadily.



Graphic correlation of postoperative activity with incidence of recurrence following hernioplasty.

#### COMMENT

Prompt postoperative ambulation has no unfavorable effect on the clinical course of patients during convalescence from hernioplasties of all types. Mean temperatures and pulse rates rise no higher and actually return to normal levels more promptly.<sup>3</sup> Local pain and discomfort are inconsequential. The average length of hospitalization may

3. Powers, J. H.: The Abuse of Rest as a Therapeutic Measure in Surgery: Early Postoperative Activity and Rehabilitation, *J. A. M. A.* **125**:1079-1083 (Aug. 19) 1944.

safely be reduced to one week or less, and the long period of convalescence which formerly followed in the wake of surgical repair may be largely eliminated.<sup>4</sup>

#### SUMMARY

After 217 hernioplasties on 210 patients who were permitted to stand, walk and sit in a chair within twenty-four hours of operation there were 115 postoperative complications—an incidence of 53 per cent. After 157 operations on 153 patients who remained in bed for an average period of 10.8 days there were 153 complications—an incidence of 98 per cent.

Of 193 hernias repaired for 161 patients who were allowed prompt postoperative ambulation it was possible to reexamine 180 from one to eight years later; there were 6 recurrent hernias—a known rate

TABLE 5.—*Incidence of Postoperative Complications and Rate of Recurrence Following Hernioplasty*

Summary Mary Imogene Bassett Hospital Complications 1933-1948	Number				
	Postoperative Activity				Total
	Prompt	Early	Late	Children	
Number of patients operated on.....	210	22	153	69	454
Number of operations.....	217	22	157	71	467
Deaths in hospital.....	0	0	15	0	15
Operative mortality (percentage).....	0	0	10	0	3
Postoperative complications (number).....	115	19	153	13	300
Incidence of complications per 100 operations	53	83	98	18	64
Recurrences 1933-1947					
Number of patients operated on.....	161	17	152	61	391
Number of hernias repaired.....	193	19	166	66	444
Number adequately followed (1 to 15 years)	180	11	129	47	367
Known recurrences .....	6	0	13	0	19
Rate of known recurrence (percentage).....	3.3	0	10.1	0	5

of recurrence of 3.3 per cent. One hundred twenty-nine hernial repairs from a total of 166 hernioplasties on 152 patients who remained recumbent in bed for eleven days after operation were reexamined one to fifteen years later; there were 13 recurrences, a known rate of recurrence of 10.1 per cent (table 5).

#### CONCLUSIONS

Many postoperative complications are favorably influenced by prompt ambulation after hernioplasty. The incidence of venous thrombosis in the lower extremities and of pulmonary infarction due to small non-fatal emboli is unaltered.

The rate of recurrence following hernioplasties of all types is significantly less among promptly ambulatory patients.

4. Powers, J. H.: Evaluation of Early Postoperative Activity, *Bull. New York Acad. Med.* 22:38-51, 1946.

## PREVENTION AND MANAGEMENT OF THROMBOEMBOLISM

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THIS report is concerned with our experience in the management of thrombosis and embolism during the past nine years at the University of Michigan Hospital. In general, our methods are not new, but through diligent and everchanging application of preventive measures, to a great extent originally described elsewhere, we are able to report marked improvement in the incidence of the grave complications which are inextricably a part of thromboembolism. It is hoped that our experience may be of help to others similarly confronted with choosing between, and in many instances employing the combined effects of, the various methods of prevention and treatment.

The incidence of pulmonary embolism has been reported to be from 1 to 12 per cent in routine autopsies in various locations and with varying types and ages of patients.<sup>1</sup> Indeed, when the entire problem is considered and those patients found to have venous thrombosis are included with those in whom embolism was the first demonstrable sign, a most conservative estimate finds evidence of thromboembolic disease in 10 per cent of necropsies.<sup>2</sup>

It is now rather generally felt that slowing of the venous blood stream, injury to the intima of veins and certain changes in the composition of the blood are most important in the development of venous thrombosis. A host of other factors known to be important, such as age, obesity, nature of the primary disease or injury, type of operation and even weather, may be considered as exerting their influence in one or more of these categories, but the exact relationship is certainly not

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Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

From the Departments of Surgery and Internal Medicine, University of Michigan Medical School.

1. Belt, T. H.: Thrombosis and Pulmonary Embolism, *Am. J. Path.* **10**:129, 1934. Breslich, P. J.: Pulmonary Embolism, *Journal-Lancet* **58**:445, 1938.

2. McCartney, J. S.: Postoperative Pulmonary Embolism, *Surgery* **17**:207, 1945.



completely understood.<sup>3</sup> In general, it appears that operations of greater duration and magnitude, especially if intra-abdominal, and particularly if in the pelvis, are accompanied with the highest incidence of thrombosis and embolism.<sup>4</sup>

The maintenance of normal physiologic processes in periods of stress, following injury or postoperatively is a goal not easily attained by the application of a few simple measures. It is imperative to avoid all measures which contribute to the impediment of normal venous return. Position of the patient in bed so that venous blood pools in the pelvis and use of pillows under the knees, as commonly employed in Fowler's position, have been condemned previously.<sup>5</sup> Similarly, the advantage of the Trendelenburg position immediately after operation has been extensively discussed.<sup>6</sup> Patients with cardiac disease, in particular those with diminished cardiac output, can be restored to more nearly normal venous return with propitious restriction of salt and use of diuretics and digitalis, with reduction of risk of thromboembolism.<sup>7</sup>

For the patient in whom venous varicosities are apparent and immobilization contemplated, the simple expedient of applying elastic compression bandages has been found to be most useful in promoting better venous return by diverting venous blood from the superficial pools through the deeper venous pathways. Friedlander<sup>8</sup> advocated use of such bandages as early as 1935. We have not found the routine use of this method to be a practical measure, and the improper application of elastic bandages without frequent readjusting is worthless.

The major role of early ambulation on the improvement of the mortality rate from thromboembolism is now clearly apparent and is well reviewed elsewhere.<sup>9</sup> The more effective treatment of abdominal

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3. Ochsner, A., and DeBaKey, M.: Therapy of Phlebothrombosis and Thrombophlebitis, *Arch. Surg.* **40**:268 (Feb.) 1940.

4. Barker, N. W.; Nygaard, K. K.; Walters, W., and Priestley, J. T.: A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism, *Proc. Staff Meet., Mayo Clin.* **15**:769, 1940.

5. de Takats, G., and Jesser, J. H.: Pulmonary Embolism: Suggestions for Its Diagnosis, Prevention and Management, *J. A. M. A.* **114**:1415 (April 13) 1940.

6. de Courcy, J. L.: Venous Stasis as Cause of Postoperative Embolism: Its Prevention by Use of Reverse Fowler Position after Lower Abdominal Operations, *Anesth. & Analg.* **8**:342, 1929.

7. Ochsner, A., and DeBaKey, M.: Therapeutic Considerations of Thrombophlebitis and Phlebothrombosis, *New England J. Med.* **225**:207, 1941. Gilbert, N. C.; de Takats, G., and Trump, R. A.: Effect of Digitalis on the Clotting Mechanism, *J. A. M. A.* **124**:736 (March 11) 1944.

8. Cited by Ochsner, A.: Intravenous Clotting, *Surgery* **17**:250, 1945.

9. Smith, L. A., and Allen, E. V.: Vascular Clinics: Studies of the Rate of Venous Blood Flow: Physiologic Studies and Relation to Postoperative Venous Thrombosis and Pulmonary Embolism, *Proc. Staff Meet., Mayo Clin.* **16**:53, 1941.

distention by means of continuous intestinal suction,<sup>10</sup> the wider application of the endotracheal tube in anesthesia, thereby extending adequate respiratory exchange to a greater number of patients, along with the encouragement of deep breathing exercises postoperatively<sup>11</sup> have all served to promote a more nearly normal flow of returning venous blood. The use of less painful transverse abdominal incisions has permitted earlier nonpainful deep respiration<sup>12</sup> and the actual insistence on exercise while the patient is in bed has undoubtedly been similarly helpful, although we have not seen fit to employ vigorous postoperative activity as recommended by Zava.<sup>8</sup>

If one is to accept Aschoff's<sup>13</sup> explanation of the origin of the venous thrombus and the view of Frykholm<sup>14</sup> and others that the thrombus is propagated in the venous stream from this original point of endothelial change, then it becomes most important to minimize damage to the venous intima by exerting great care when operating in the region of venous pathways. In a previous communication emphasis was placed on avoidance of performing venipuncture in veins of the leg.<sup>15</sup>

The major cause of death in fractures about the hip has been reported to be pulmonary embolism,<sup>16</sup> and prophylactic ligation following this injury has been advised for this reason.<sup>17</sup> Intimal injury to the large veins at the time of fracture, in addition to the slowing of the venous stream by edema, extravasation and immobilization, appears to be the predisposing factor in injuries of this region.

In severe crushing injuries, extensive operative procedures and also in widespread carcinoma undoubtedly many factors contribute to the

10. Bellis, C. T., and Wangenstein, O. H.: Venous Circulatory Changes in Abdomen and Lower Extremities Attending Intestinal Distention, *Proc. Soc. Exper. Biol. & Med.* **41**:490, 1939.

11. Patey, D. H.: The Effect of Abdominal Operations on the Mechanism of Respiration, with Special Reference to Pulmonary Embolism and Massive Collapse of the Lungs, *Brit. J. Surg.* **17**:187, 1930; Artificially Induced Thrombophlebitis with Suggested New Approach to Problem of Postoperative Pulmonary Embolism, *Surg., Gynec. & Obst.* **64**:1002, 1937.

12. Coller, F. A., and Maclean, K. F., in *Tribute to Lloyd Noland by Employees Hospital Reunion Committee*, 1947.

13. Aschoff, L.: *Thrombosis: Lectures in Pathology*, New York, Paul B. Hoeber, 1924.

14. Frykholm, R.: The Pathogenesis and Mechanical Prophylaxis of Venous Thrombosis, *Surg., Gynec. & Obst.* **71**:307, 1940.

15. Lillie, R. H.: Pulmonary Embolism, *Univ. Hosp. Bull., Ann Arbor* **10**:93, 1943.

16. Golodner, H.; Morse, L. T., and August, A.: Pulmonary Embolism in Fractures of the Hip, *Surgery* **18**:418, 1945.

17. Allen, A. W.; Linton, R. R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism: Further Experience with Thrombectomy and Femoral Vein Interruption, *J. A. M. A.* **128**:397 (June 9) 1945.

increased incidence of thromboembolism, possibly through the liberation of large amounts of thrombokinase.<sup>18</sup> Other changes in the blood reflected in the varying response to the administration of heparin sodium<sup>19</sup> and to variation in prothrombin concentration<sup>20</sup> have been correlated with the development of venous thrombosis and as a result have been suggested as possible prognostic tests for impending or early thromboembolism. We have not found any of these measures to be sufficiently practical for general clinical use.

Coincident with the widespread acceptance of many of the precautionary measures just mentioned have come reports of an unchanged incidence of venous thrombosis and pulmonary embolism.<sup>21</sup>

It has been most difficult to estimate the frequency with which venous thrombosis has occurred among our patients for several reasons. No doubt our acuity in making and willingness to make this diagnosis have increased rapidly in the past nine years as we have become more aware of the significance of thromboembolic disease. In similar manner it is felt that the pathologists have increased their ability to find an offending thrombus by examination of the veins of the lower extremities at autopsy. A third factor influencing the statistics on the frequency of venous thrombosis has been the insistence on the early application of preventive ligation and anticoagulant therapy, which has necessarily made it impossible to confirm the presence of venous thrombosis as the process was not allowed to reach its fully developed stage.

It has been encouraging to note the decline in the total incidence of pulmonary embolism among our patients as illustrated in chart 1. Since our active program of prevention began with venous ligation in cases of suspected or well developed venous thrombosis in the latter months of 1943, it is of interest that comparison of the incidence of pulmonary embolism for the last four year period shows a decrease from 169 to 53 cases (emboli being 31 per cent as frequent) when compared with a four year control period (chart 2), when only general measures were employed in the treatment of venous thrombosis. Among the patients with pulmonary embolism in the two four year periods, the mortality rate has not appreciably changed, being 38 per cent in the first four years and 42 per cent in the last four years.

Of great concern has been our apparent failure to improve the chances that the patient with cardiac disease will avoid thromboembo-

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18. de Takats, G., and Fowler, E. F.: The Problem of Thrombo-Embolism, *Surgery* **17**:153, 1945.

19. de Takats, G., and Fowler, E. F.: Heparin Tolerance, *Surg., Gynec. & Obst.* **77**:31, 1943.

20. Sandrock, R. S., and Mahoney, E. B.: Prothrombin Activity, *Ann. Surg.* **128**:521, 1948.

21. Roe, B. B.: To be published.

lism. Although many more pulmonary emboli occur among surgical patients (222 in the eight year period 1940 to 1947 compared with 71 among medical patients), it is interesting to correct these figures for hospital admissions. During this period 24,637 patients were admitted to the medical wards and 75,031 to the surgical wards. The incidence

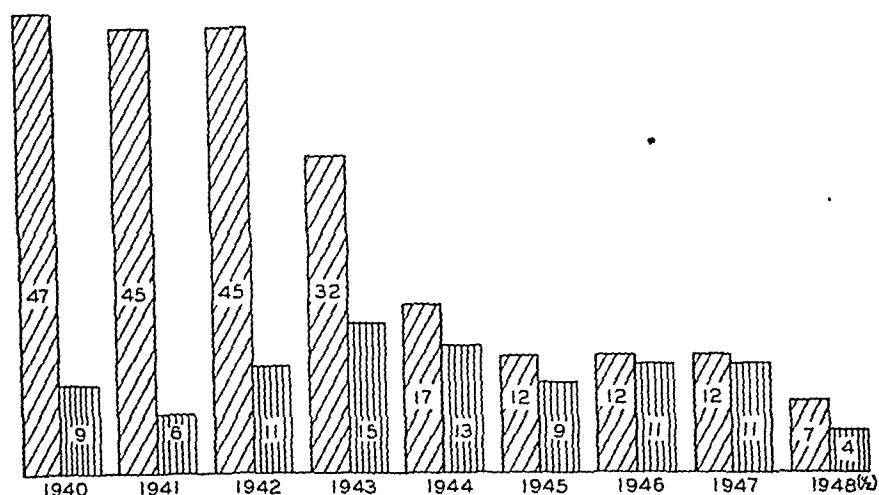


Chart 1.—Incidence of pulmonary embolism at the University of Michigan Hospital. The column at the left for each year indicates the number of patients without cardiac disease; that at the right, the number with cardiac disease.

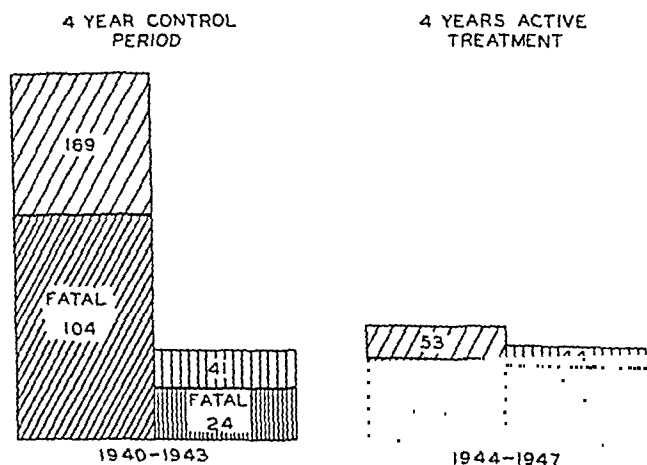


Chart 2.—Comparative incidence of pulmonary embolism. The column at the left for each period indicates the number of patients without cardiac disease; that at the right, the number with cardiac disease.

of pulmonary embolism is thus 2.96 per thousand among surgical admissions and 2.88 per thousand among nonsurgical admissions.

In reviewing the incidence of pulmonary embolism grouped according to the patient's primary disease, one finds the greatest number of

emboli occurring among the general surgical patients (chart 3). However, if one includes the patients with cardiac disease and corrects the incidence for numbers of patients admitted to each service, then the incidence is noticeably changed and it is the medical and, more particularly, the patient with cardiac disease who appears most vulnerable



Chart 3.—Incidence of pulmonary embolism by service among patients without cardiac disease.

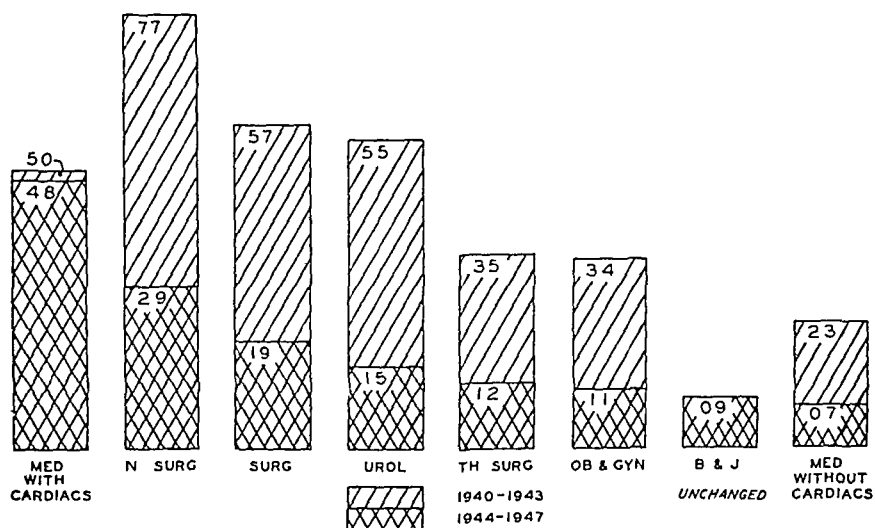


Chart 4.—Incidence of pulmonary embolism per thousand patients admitted to the hospital.

(chart 4). It is of interest that the medical patients without cardiac disease have demonstrated a sharp fall in thromboembolic disease similar to the improvement seen throughout the hospital. Again, it is obvious that little has been done for the patient with cardiac disease in reducing the incidence of venous thrombosis and embolism.

Since prevention of femoral-iliac-caval thrombosis has not been totally accomplished by the widely used general precautionary measures now employed, one must accept the possibility that further reduction in incidence of this disease may occur only after the protective use of venous ligation or the preventive use of anticoagulants. The use of either method alone or in combination on every patient admitted to the hospital as a means of prophylaxis seems hazardous and ill advised. On the other hand, to choose only those patients with specific diseases or those about to be subjected to specifically designated operations may be undesirable in many instances. In addition, the methods advocated and used successfully by some physicians may not be suitable to facilities available to others. Prophylactic measures must then be simple, readily available and effective. They must not affect adversely the primary disease; they must not be allowed to interfere with or complicate the desired treatment essential for the primary disease, and the morbidity and mortality associated with this prophylactic measure must be minimal.<sup>22</sup>

#### ANTICOAGULANTS

Heparin sodium has been employed in thrombosis, in embolism and after myocardial infarction when an immediate anticoagulant effect has appeared desirable. Usually the drug was continued until the prothrombin concentration had been substantially reduced (30 per cent or lower) by dicumarol,<sup>®</sup> the initial dose of which was given coincident with the first dose of heparin. The danger of thromboembolism in this "critical" period, following the initiation of dicumarol<sup>®</sup> therapy, is not easily estimated. In our experience, thromboembolism, progressive thrombosis or a repeated pulmonary embolus has appeared in a few instances prior to the obtaining of effective prothrombin levels with dicumarol.<sup>®</sup> This has led us to favor the more frequent use of heparin initially.

Heparin sodium has been administered intravenously either by continuous infusion<sup>23</sup> (100 to 200 mg. in 1,000 cc. of 5 per cent dextrose solution) or intermittently<sup>24</sup> (50 to 100 mg. at four to six hour intervals). In addition, a group of patients received intermittent intramuscular injections of heparin sodium.<sup>25</sup> If the drug is given by continuous infusion, care must be observed to control the flow at a uniform rate. The intermittent treatment, although more expensive and difficult

22. Collier, F. A.: Thrombo-Embolism, editorial, *Surgery* **17**:315, 1945.

23. Murray, D. W. G., and Best, C. H.: Heparin and Thrombosis: Present Situation, *J. A. M. A.* **110**:118 (Jan. 8) 1938.

24. Crafoord, C., and Jorpes, E.: Heparin as a Prophylactic Against Thrombosis, *J. A. M. A.* **116**:2831 (June 28) 1941.

25. Walker, J.: The Efficacy of Heparin Administered by Intravenous, Intramuscular and Subcutaneous Routes, *Surgery* **17**:54, 1945.

to carry out over a prolonged period, is preferable for a patient in whom a continuous thirty-six to forty-eight hour infusion may be impractical.

Although, to some extent, the dosage requirements of heparin are related to body weight, they can be estimated only by the frequent determinations of the blood-clotting time. For this purpose, we have used the Lee and White test by which values up to eleven minutes are normal. Though we have no proof that control of a thromboembolic process is necessarily favored when the dosage of heparin is regulated by clotting tests, performance of such tests prior to the start of treatment and at least once daily thereafter is recommended as a safeguard against excessive prolongation of the clotting time. An adequate heparin effect has been obtained, in our opinion, when the clotting time has been doubled (fifteen to twenty-five minutes). Since heparin produces enormous prolongation of the prothrombin time, care must be observed to obtain blood for determinations of prothrombin time (in estimating the dosage of dicumarol<sup>®</sup>) three to four hours after the last dose of heparin. Heparin does not generally appear to hasten the reduction of prothrombin by dicumarol.<sup>®</sup> As prothrombin activity is reduced by dicumarol,<sup>®</sup> however, increased sensitivity to heparin may be anticipated.

Heparin sodium occasionally induces a mild foreign protein reaction or it may produce hematuria and wound hemorrhage. The incidence of these complications is considerably less than that of the complications associated with dicumarol.<sup>®</sup> Since the effect of heparin is limited to a three to four hour period, minor cases of bleeding may be expected to cease spontaneously. Intravenous injection of protamine sulfate may also be employed quickly to reverse the effect of heparin, and blood transfusion is indicated in the event of severe bleeding. Vitamin K is of no value to reverse the effect of heparin.

Dicumarol<sup>®</sup> must be given orally and is available in 50 and 100 mg. capsules. Soon after ingestion it is rapidly removed from the stomach or upper gastrointestinal tract. Reduction of the prothrombin content of peripheral blood is the only known physiologic effect of dicumarol.<sup>®</sup>

Adequate facilities for measuring prothrombin are essential for the safe and effective administration of dicumarol.<sup>®</sup> The Quick procedure has proved eminently successful for this purpose. By the unmodified Quick test, employing whole plasma and potent thromboplastin (of which there are several reliable commercial sources), the normal prothrombin time is remarkably constant, varying from twelve to sixteen seconds (assumed to represent 100 per cent prothrombin concentration). Prothrombin activity may be expressed in terms of seconds of "prothrombin time," or as percentage of prothrombin (calculated from the formula 
$$\frac{\text{normal prothrombin time [seconds]}}{\text{patient's prothrombin time [seconds]}} \times 100$$
) or, after interpolation from a prothrombin dilution curve, as "percentage of normal prothrombin concentration."

We have preferred to express prothrombin activity in terms of percentage of normal concentration. By this method the effective range of concentration, through practical experience, has been found to be less than 30 per cent and greater than 10 per cent. It is evident that thromboembolism is less common at concentrations below 30 per cent. Utilization of this expression of prothrombin activity implies the construction of frequent dilution curves, which, for the small laboratory, is difficult if not impossible. In these circumstances it is agreed that the preferable expression of prothrombin activity is in seconds of "prothrombin time." The clinician must always be informed of the prothrombin time of the control (normal) plasma as well as that of his patient. Reasonable daily consistency of the control value (variation not in excess of four seconds) is imperative and is the key to the safe administration of dicumarol.<sup>®</sup> When this is assured, the drug may be given to prolong the patient's prothrombin time to values twice the control but not in excess of thirty-five seconds. Such values, for practical purposes, compare favorably with the effective range of prothrombin concentration (10 to 30 per cent).

Dicumarol<sup>®</sup> is usually given initially as a single 300 mg. dose, following a pretreatment determination of prothrombin concentration. Thereafter, the dosage must always be estimated on the basis of daily prothrombin determination. When this is expressed in terms of percentage prothrombin concentration, from 100 to 200 mg. of the drug, dependent on the patient's response, is given each day that the concentration is 20 per cent or above; the drug is withheld when the concentration is below 20 per cent.

In our experience prothrombin concentration will be reduced by dicumarol<sup>®</sup> to the therapeutic range in an average of 2.8 days. The initial effective dosage of dicumarol<sup>®</sup> proved to be about 600 mg.; approximately 900 mg. was administered in the first week of treatment, and the average total dose (to obtain about ten days of effective prothrombin levels) was 1,400 mg. Six days after the last dose of dicumarol<sup>®</sup> the prothrombin was usually found to be elevated to the normal range (70 to 100 per cent prothrombin concentration).

There is considerable variation in sensitivity to dicumarol<sup>®</sup> not reflected by these figures. The time required to obtain an effective level was not materially lessened unless the pretreatment prothrombin level was in the range of 50 per cent concentration or below, when an effective level was obtained in about 1.7 days. About 10 per cent of our patients with normal pretreatment prothrombin levels were reduced to 30 per cent prothrombin concentration within twenty-four hours by a single 300 mg. dose of dicumarol.<sup>®</sup> By way of contrast, in about the same percentage of cases from 1,000 to 1,800 mg. of dicumarol<sup>®</sup> was required before the effective range was reached.



We have observed increased sensitivity to dicumarol® in patients with major hepatic or renal insufficiency; in some patients with cardiac failure, and on two occasions in patients with severe acidosis and alkalosis. In occasional patients dicumarol® induces nausea, vomiting and abdominal cramps. Low prothrombin levels may be associated with a distinct feeling of malaise and fatigue.

Effective levels of prothrombin were maintained about 6.5 days in the average postoperative patient to whom dicumarol® was given prophylactically; treatment was usually instituted on the first or second postoperative day. About ten days of effective prothrombin concentration levels were maintained in patients with peripheral venous thrombosis. Similar concentrations for two weeks are advised in patients

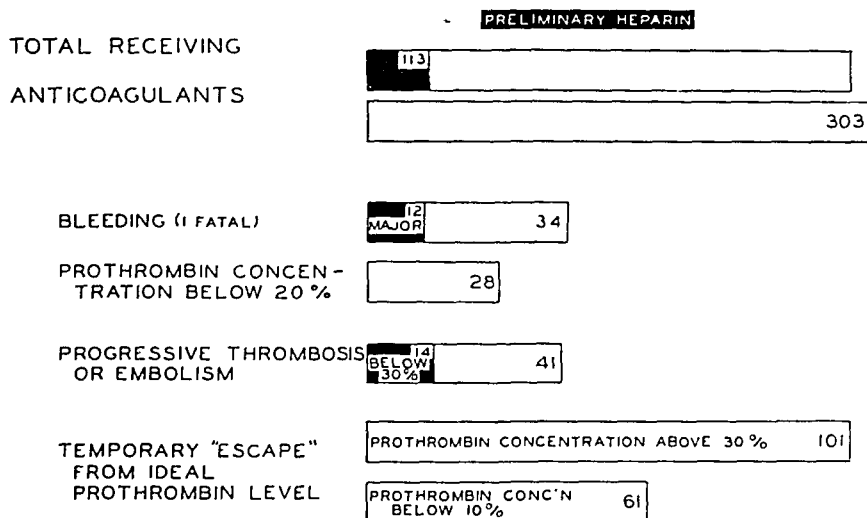


Chart 5.—Complications of anticoagulant therapy.

with pulmonary infarction and from three to four weeks in patients with myocardial infarctions.

Perfect control of prothrombin concentration in the effective range should not be expected with dicumarol®. In our experience with 303 patients (chart 5), temporary and accidental escape of prothrombin above the 30 per cent concentration occurred at some time in 101 (33 per cent) of the cases. An average of 300 mg. of the drug was required to correct such a rise. In a few cases, in these circumstances, thromboembolism may be expected to progress.

Temporary decline of prothrombin levels to less than 10 per cent concentrations occurred in 61 (17 per cent) of the patients after an average of 850 mg. of dicumarol® and persisted for an average of 1.5 days. The fact that in less than 10.5 per cent of these patients there was bleeding emphasizes that hypoprothrombinemia of this magnitude

need not be viewed with alarm. If spontaneous correction has not occurred within twenty-four hours, vitamin K should be administered, a single intravenous injection (72 mg. of menadione sodium bisulfite) being usually sufficient.

Every physician administering dicumarol® should realize that reduction of prothrombin to effective levels is associated with a definite incidence of bleeding, averaging 11 per cent in our experience. The prophylactic use of the drug in postoperative patients is associated with an increase in the incidence (16 per cent) and severity (in 6 of 10 cases bleedings were major in extent) of this complication. In two thirds of the cases hemorrhage occurred at a prothrombin concentration of less than 20 per cent and in one fifth in the range below 10 per cent. The severity of bleeding is not necessarily related to the prothrombin level at which it occurs, and patients should not be discharged from the hospital until the prothrombin concentration is above 50 per cent.

The physician responsible for the administration of dicumarol® should be prepared in the event of severe or persistent hypoprothrombinemia and severe or persistent bleeding to reverse its effect by large doses of vitamin K. We recommend in the event of excessive bleeding that 72 mg. of vitamin K (menadione sodium bisulfite) be given intravenously every four hours for four to six doses or until the bleeding ceases. In the average case of minor bleeding, in our experience, an average of 185 mg. of vitamin K was required; in cases of major bleeding an average of 272 mg. was required before bleeding ceased. Such large doses have not been associated with toxic effects. In the event of severe hemorrhage, blood transfusions should be freely used to supplement vitamin K.

From our experience with the 1,150 patients who form the background of the study, the following indications for the use of the chemical anticoagulants as active prophylactic measures may be outlined.

*Prophylactic Anticoagulant Therapy (No Venous Thrombosis)*

1. Recent episode of thromboembolism; immobilization contemplated
2. Severe contusions of the lower limbs
3. Obesity; immobilization contemplated
4. Retroperitoneal tumor
5. Operation in the region of major vessels
6. Arterial embolism
7. Transverse myelitis
8. Pelvic inflammation
9. Varicose veins, untreated
10. Congestive heart failure; myocardial infarction

It is difficult to define the "safe" period for a given patient when freedom from pulmonary embolic episodes may be expected following

venous thrombosis. Treatment of every patient with a suspected history of venous thrombosis within his lifetime would be unfeasible. However, one can say that any patient who has had a previous episode of thrombosis or embolism within the past year and is facing operation or prolonged rest in bed should not be denied active preventive measures. For those patients who have had a manifestation of thromboembolism many years previously, the general preventive measures described earlier should be assiduously applied and early treatment carried out if thrombosis or embolism appears.

Direct trauma to blood vessels is an obvious cause of intravascular clotting. In other instances propagation of the thrombus from the site of injury into the major veins of the extremity may occur. The increase in formed elements of the blood and its increased coagulability as a result of tissue damage also favor the production of a thrombus. An ideal set of circumstances then exists when, in addition to these factors, the part is immobilized in a plaster cast or in a complicated traction apparatus. That intravenous clotting does not always occur in such instances is not easily explained.

The role of obesity as a factor predisposing to thrombosis is difficult indeed to evaluate.<sup>26</sup> Certainly the loss or diminution in the vascular tone of obese patients may accentuate slowing of the blood stream when inactivation is necessary. Many of these persons have a considerably reduced range of pulmonary excursion in the supine position. It seems more than coincidence that a vast number of patients in whom intravascular clotting occurs are obese. For an extremely obese person, when an extensive operative procedure and immobilization are planned prophylactic use of anticoagulants might well be considered.

A large number of the tumors occurring in or extending to the retroperitoneal area will result in progressive venous obstruction. Increasing weakness, lethargy and inactivity may aid in the deposition of a soft thrombus in the extremities of such patients. Before the tumor completely occludes the major venous channels, a massive pulmonary embolus resulting in the death of the patient may intervene. When reasonable palliation or curative therapy is contemplated for such tumors, measures to prevent this accident should be carried out. Venous ligation is usually technically unfeasible in such patients.

Operations such as inguinal and iliac lymphadenectomy, combined abdominoperineal resection and urinary cystectomy which are performed in the immediate vicinity of great vessels are also often instances of direct trauma that result in the intimal damage responsible for the inception of a venous thrombus. The injury to soft tissues resulting from these and other more or less extensive operations and the changes

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26. Snell, A. N.: Relation of Obesity to Fatal Pulmonary Embolism, *Arch. Surg.* **15**:237, 1927.

occurring in the blood constituents which appear in long and difficult procedures favor the progression of such a nidus.

The profound ischemia or inadequate dilatation of collateral arteries induced by the vasospasm after sudden arterial occlusion produces changes in the intima of both arteries and veins which if prolonged result in widespread thrombosis. Therefore, treatment of the patient with acute arterial occlusion should include not only the relief of vascular spasm and arterial obstruction by embolectomy when possible but also the prevention of extending venous thrombosis by the administration of anticoagulants. In arterial embolism, the lapse of time prior to relief of occlusion is of greatest importance from the standpoint of both viability of the part and extension of the thrombosis, and after embolectomy the administration of anticoagulants should be instituted.

Patients with complete transection of the spinal cord usually have loss of normal vasomotor responses and, as a result, a warm, dry extremity with maximal vasodilatation. Because of this fact, many observers have considered phlebothrombosis as an unlikely complication in this group of patients. Schneider<sup>27</sup> followed 58 such patients in a service-connected neurosurgical service and found the death of one patient due to a pulmonary embolus. Ten patients in the series under consideration exhibited evidence of thromboembolism following transverse myelitis. Six of these patients died with massive or multiple, recurring pulmonary emboli.

The use of anticoagulants in this type of patient should be withheld until the danger of continued bleeding into the traumatized spinal cord or from the site of surgical exploration is no longer present. In most instances, anticoagulants may be begun as early as forty-eight hours after injury or operation. Ligation of the inferior vena cava seems an acceptable alternative, provided it can be carried out early and without endangering the patient's recovery. Anticoagulant prophylaxis should be continued until the patient is no longer restricted to bed, which for a large number of patients will be approximately three months following injury. Those patients requiring longer immobilization should be offered the protection of ligation of the vena cava. In the face of complications necessitating immobilization of an already ambulatory patient, ligation of the vena cava or a repeated course of anticoagulants is suggested as the best protection against massive fatal pulmonary embolism.

Mechanical or infectious trauma to pelvic veins frequently occurs after pelvic laparotomy, in the postpartum period, after a difficult labor, instrumental delivery or cesarean section and in the presence of puerperal sepsis or other forms of widespread pelvic inflammatory disease. Often these patients are immobilized in bed for a long time, and pelvic

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27. Schneider, R. C.: Personal communication to the authors.

trauma is a potential source for the development of an extending venous thrombosis. Allen, Barker and Hines<sup>28</sup> have cited an incidence of pulmonary embolus from 1.25 to 12.5 per cent after gynecologic operations.

Meisen<sup>29</sup> has stated that 10 to 17 per cent of the general population have varicose veins and after the age of 20 the incidence in women is approximately four times that in men. The development of varicosities in obese persons is considerably enhanced. In the large, saccular superficial veins pooling of blood readily occurs when the extremity is dependent or light pressure is exerted above the varix. Intimal sclerosis and inflammatory infiltration in the perivenous tissues are common histologic observations. Thus, stasis and intimal damage, two of the three commonly accepted prerequisites of intravascular clotting, are already present in these patients. Once clotting is initiated, extension through the communicating vessels into the major venous trunks is readily accomplished, although this is by no means the commonest manner in which femoral thrombosis is initiated.

Surgical extirpation of varicose veins is the only certain means of eliminating them as a source of future thrombosis. The application of compression bandages to the lower extremities to obliterate the superficial veins is often adequate but equally often is an unreliable means in our experience of accomplishing the same end. When definitive treatment, such as surgical extirpation, cannot be accomplished because of the urgency of the patient's disease, anticoagulant prophylaxis is a useful means of preventing thrombosis.

The incidence of thromboembolism as a complication of coronary thrombosis with myocardial infarction has been reported as varying from 37 per cent on the basis of clinical findings<sup>30</sup> to 45 per cent in autopsy cases.<sup>31</sup> By the prompt institution of anticoagulant therapy after a myocardial infarction, it is hoped that the formation of mural thrombi and subsequent embolic showers may be forestalled. The anticoagulants may serve to halt the extension of the initial coronary thrombosis by propagation as well as the formation of new thrombi in other coronary branches and to prevent the development of thromboses in the pelvic and leg veins, from which the majority of fatal pulmonary emboli have their origin.<sup>32</sup> The recently reported cooperative study of

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28. Allen, E. V.; Barker, N. W., and Hines, E. A.: *Peripheral Vascular Diseases*, Philadelphia, W. B. Saunders Company, 1946, p. 592.

29. Meisen, V., cited by Allen, Barker and Hines,<sup>28</sup> p. 665.

30. Nay, R. M., and Barnes, A. K.: Incidence of Embolic or Thrombotic Processes During Immediate Convalescence from Acute Myocardial Infarction, *Am. Heart J.* **30**:65, 1945.

31. Hellerstein, H. K., and Martin, J. W.: Incidence of Thrombo-Embolic Lesions Accompanying Myocardial Infarction **33**:443, 1947.

32. Nichol, E. S.: Treatment of Acute Coronary Thrombosis with Dicumarol: Further Observations, *Am. Heart J.* **33**:722, 1947.

the American Heart Association<sup>33</sup> indicates that by the proper use of anticoagulant therapy the mortality rate of coronary thrombosis can be reduced from approximately 23 per cent (control series) to 13 per cent and the incidence of thromboembolic complications from approximately 19 per cent to 9 per cent. Our experience, in a small series of patients with myocardial infarctions, is in agreement with these figures. Although this form of treatment, as the figures indicate, is not completely protective, it is recommended that, for the most part, every patient with a myocardial infarction be given the benefit of anticoagulant therapy.

There is need to put into practice measures which will aid in reducing the frequency and gravity of thromboembolism as a complication of other forms of heart disease. Carlotti and co-workers,<sup>34</sup> in a study dealing with the problem of pulmonary embolism among medical patients at the Massachusetts General Hospital over a ten year period, reported that from 59 to 71 per cent of pulmonary embolisms occurred in patients with cardiac disease, especially the rheumatic, hypertensive and coronary forms. Auricular fibrillation was present in nearly one third, and congestive failure was frequently present. In patients with massive pulmonary embolism in whom the leg veins were examined at autopsy, 75 per cent showed thrombosis. Thrombi were found in the right side of the heart in relatively few. In cardiac failure the development of thromboembolism is favored by the increased viscosity of the blood associated with the hemoconcentration accompanying shock and by venous stasis concomitant with decrease in cardiac output.<sup>35</sup> Venous dilatation on the basis of obstruction, decrease in movement of the legs with enforced rest in bed and limitation of respiratory excursion further increase peripheral venous stagnation. Venous thrombi, in these circumstances, must be masked many times by peripheral edema.

White<sup>35</sup> has stressed that in a patient with cardiac disease with congestive failure who fails to respond as he should to treatment the commonest complication is pulmonary embolism and infarction, easily overlooked and often diagnosed incorrectly. In our experience with 15 such patients, it appeared that the majority had sustained at least one infarction before admission to the hospital. The fact that definitive treatment was not instituted in these patients for an additional period of five days following admission indicates the general lack of awareness of the frequency and gravity of pulmonary embolism in these patients.

33. Wright, I. S.; Marple, C. D., and Beck, D. F.: Anticoagulant Therapy of Coronary Thrombosis, *J. A. M. A.* **138**:1074 (Dec. 11) 1948.

34. Carlotti, J.; Hardy, I. B.; Linton, R. R., and White, P. D.: Pulmonary Embolism in Medical Patients, *Am. Heart J.* **33**:737, 1945.

35. White, P. D.: *Heart Disease*, ed. 3, New York, The Macmillan Company, 1947, p. 635.

Recognizing that much of the thromboembolism in cardiac and other serious diseases is terminal, it still appears likely that much might be done to reduce the gravity of the problem. Prophylactic interruption of the femoral vein has been recommended when pulmonary embolism is discovered in patients with cardiac disease.<sup>34</sup> Homans<sup>36</sup> stated: ". . . if, in any instance of heart disease in which confinement to bed for more than a week is expected, embolism is believed to have occurred (from thromboses clinically evident or presumed to be present in the lower limbs), both common femoral veins should be explored and ligated. When there are actual contraindications for the anticoagulants, such a rule may be counted imperative; otherwise it is a matter for professional experience and judgment to determine." Although patients in congestive failure sometimes prove unusually sensitive to dicumarol,<sup>®</sup> we prefer the more extensive use of prophylactic anticoagulant therapy to venous ligation in this group. We are aware, moreover, that the mortality rate is still considerable despite either course of action. In our experience, despite effective concentrations of prothrombin, death occurred in 33 per cent of the patients with cardiac disease complicated by congestive failure and pulmonary infarction. By comparison, the mortality rate was 28.3 per cent in a group of 60 patients treated by ligation in Carloti's series, and in the control group of 213 patients treated without ligation the mortality rate was 50.7 per cent.

It is becoming evident that special indications for long range prophylactic anticoagulant therapy may exist in some patients with heart disease. Wright,<sup>33</sup> in particular, emphasized these benefits in the case of the patient with old rheumatic heart disease, auricular fibrillation and intracardiac thrombi from which showers of emboli have occurred.

#### *Contraindications to Anticoagulants*

1. Lack of adequate laboratory control
2. Extreme old age (variable)
3. Repeated infarction, progressive thrombosis or major hemorrhage during anticoagulant therapy
4. Recent cerebrovascular accident
5. Major renal or hepatic damage
6. Ulcerative or granulating lesions, potential source of extensive bleeding
7. Central nervous system lesions after operation or constituting special bleeding risk
8. Obstetric conditions in which bleeding is a major hazard
9. Blood dyscrasias with a bleeding tendency
10. Subacute bacterial endocarditis

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36. Homans, J.: Operative Treatment of Venous Thrombosis in the Lower Limbs, *Am. J. Med.* 3:345, 1947.

Several of the important contraindications to anticoagulant therapy are outlined in the preceding tabulation. The most important obstacle to the widespread use of dicumarol® is lack of satisfactory laboratory tests to measure prothrombin activity. It cannot be too greatly stressed that administration of the drug is almost by necessity limited to hospitalized patients and in the absence of reliable prothrombin tests is ill advised.

Patients with severe hypertension and known past cerebrovascular accidents are poor risks for anticoagulant therapy; fatalities in these circumstances have occurred in our experience. Anticoagulant therapy has been employed in some carefully selected cases of cerebral thrombosis. It is questionable whether the beneficial results of this form of treatment are significant or constant enough to justify the involved risks.

Dicumarol® is believed to reduce prothrombin activity through its effect on the liver, and both dicumarol® and heparin are presumably eliminated in part by the kidneys. Major impairment of renal and hepatic function definitely increases sensitivity to dicumarol®, and some patients with congestive failure are likewise sensitive, presumably on the basis of reduced renal blood flow. In these circumstances heparin and dicumarol® should be employed with caution.

Anticoagulant therapy is further contraindicated in patients with known but inaccessible ulcerative, granulating or bleeding lesions which constitute a potential source of extensive bleeding. Such lesions are commonly encountered in the gastrointestinal tract.

Recent surgical procedures on the eye or on the central nervous system or on its lesions constitute special contraindications to anticoagulants from the fact that a small amount of bleeding in these circumstances conceivably could produce irreversible damage. In a variety of special gynecologic and obstetric situations in which bleeding is a prominent feature the use of anticoagulants would be unwise. These drugs should be employed with caution in the last trimester of pregnancy.

Patients with blood dyscrasias, with a bleeding tendency, are poor risks for anticoagulant therapy. Subacute bacterial endocarditis, with its increased bleeding tendency, has generally come to be recognized as a contraindication to the use of heparin and dicumarol®, and an appreciable percentage of the deaths attributed in the literature to the latter drug have occurred in patients with subacute bacterial endocarditis.

#### VENOUS LIGATION

In discussing venous ligation it will be pointed out that patients facing an imminent operation and the very elderly person might best have their venous thrombosis treated with vein ligation to obviate hemorrhagic risks attending anticoagulant therapy.



Now that some of the enthusiasm for ligation of the femoral vein has abated, it is well to attempt to evaluate its place in the prevention and treatment of thromboembolism.

There are many physicians who feel that, because a fresh venous thrombus is only loosely attached to the vein wall, it is imperative that either thrombectomy or ligation of the vein above the thrombus be carried out at once whenever the diagnosis of phlebothrombosis is made. Ochsner<sup>37</sup> has expressed the belief that this procedure should take precedence over every other operative procedure except measures to combat massive hemorrhage.

The technic of ligation of the femoral and iliac veins and the inferior vena cava have been described in detail elsewhere.<sup>38</sup> Whenever ligation of a femoral vein was indicated and a thrombus was found extending into the common femoral vein, an attempt was made to ligate above the clot. Thus, ligations of the superficial femoral vein were done, for the most part, when no clot was detectable above this level. Thrombectomy was performed in all cases in which it was possible to demonstrate a clot. Ligations of the inferior vena cava have been carried out through a retroperitoneal approach, the vessel being ligated in continuity and above the clot.

When the major failures of vein ligation are reviewed (chart 6), however, some reconsideration of its widespread application is necessary. The primary reason for concern in patients with phlebothrombosis is the occurrence of pulmonary embolism; in 10 of our patients embolism occurred after ligation was carried out, an incidence of 6 per cent of failure of protection. More disturbing are the cases of the 3 patients in whom a fatal massive pulmonary embolus occurred in the postligation period. Two of these patients had only a unilateral femoral ligation, but in the third both superficial femoral veins were ligated. This is an object lesson indeed for those who feel that bilateral ligation offers complete protection from pulmonary embolism. Four patients on whom ligations were carried out had one or more subsequent embolic episodes which contributed to their deaths. Again, complete protection was anticipated in 1 of these when the inferior vena cava was ligated. In this patient recurring pulmonary emboli appeared after anticoagulant therapy, and he was critically ill at the time of subsequent caval ligation. The postligation embolus would undoubtedly have been non-fatal in a less debilitated person. In the 3 patients who had minor emboli after ligation, only unilateral ligations were done and it is sus-

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37. Ochsner, A.: *Venous Thrombosis, Surgery* 24:445, 1948.

38. Homans, J.: *Exploration and Division of the Femoral and Iliac Veins in the Treatment of Thrombophlebitis of the Legs*, *New England J. Med.* 224:179, 1941. Northway, R. O., and Buxton, R. W.: *Ligation of the Inferior Vena Cava*, *Surgery* 18:85, 1945.

pected that the subsequent emboli originated in the opposite leg. In 1 patient hemorrhage during ligation necessitated postponement of the ligation. Subsequently, this was accomplished without event.

Extreme postligation edema has been suggested as a serious complication by Dennis.<sup>39</sup> We have not seen it seriously endanger the extremity of a patient, but in 1 of our patients bilateral ligations were carried out on separate occasions and each ligation was followed by tremendous edema of the leg. It is interesting to note that the superficial femoral and greater saphenous veins were ligated on one side, while the common femoral and saphenous veins were ligated on the other.

Despite the obvious failure in a few instances of ligation of femoral or iliac veins or of the vena cava to protect against embolic accidents,

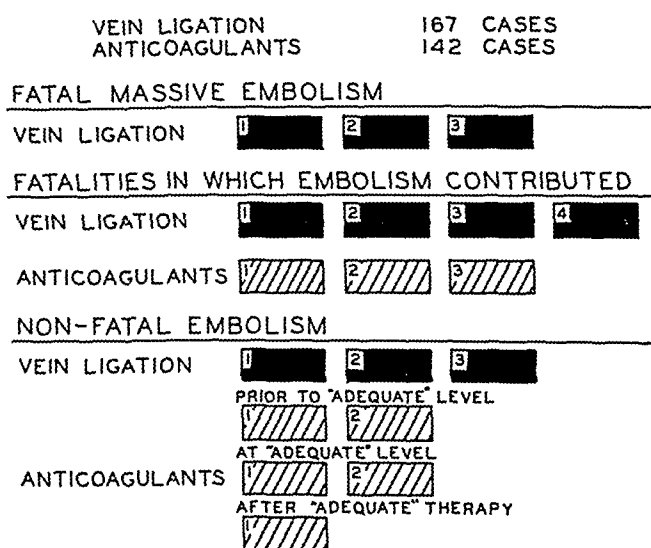


Chart 6.—Failure of prevention of pulmonary embolism in cases of venous thrombosis.

there is a definite need and place for this procedure in the treatment of phlebothrombosis. It must be emphasized, however, that ligation below the level of the inferior vena cava must be bilateral to be adequate. It seems likely that many of the cited evidences of failure were due not to the ineffectiveness of the method but to the fact that the ligations were unilateral.

The most obvious need for ligation lies in those instances in which the use of anticoagulants is contraindicated, regardless of whether the contraindication is technical in that laboratory facilities are unavailable or whether the contraindications are specifically medical, as in a patient who is bleeding.

39. Dennis, C.: Disaster Following Femoral Vein Ligation for Thrombophlebitis, *Surgery* 17:264, 1945.

Venous ligation is often a necessary alternative in patients with septic thromboembolism. In such instances thrombosis in small vessels may be an important part of the defense mechanism of the body which prevents uninhibited extension of the suppurative process. In such instances the choice between ligation and anticoagulants will depend largely on the sensitivity response of the infecting organism to the antibiotic and chemotherapeutic agents.<sup>40</sup> If the organism should prove unresponsive to these agents, the anticoagulants would be undesirable and vein ligation could be effectively substituted. On the other hand, when the infecting organism responds readily to the available antibacterial agents or when the suppurating focus can be readily excised,<sup>41</sup> control of progressive thrombosis may be suitably carried out by anticoagulants.

In thrombosis of the saphenous vein proximal saphenous ligation accompanied with early ambulation seems to us to be the simplest effective treatment. Anticoagulant therapy in this instance may be hazardous and usually no more effective.

Absolute contraindication to ligation of either the superficial or the deep venous systems exists only when the desired ligation site is compromised by an extensive burn, infection or neoplasm.

The frequency of pulmonary complications following amputations of a leg was estimated by Veal to be 14.9 per cent in the 275 cases which he reviewed,<sup>42</sup> and he stated that many of these pulmonary lesions were embolic in origin. DeTakats, in his discussion of Veal's paper, noted that in 110 patients undergoing major amputations in his experience between 1927 and 1942 there was 1 who died of a pulmonary embolus following amputation.

At the University of Michigan Hospital 373 amputations of the leg were performed between 1939 and 1948 and 6 patients during this period had pulmonary emboli following amputation, an incidence of 1.6 per cent. Because of our concern for the risk of embolism in our patients on whom amputation has been carried out, prophylactic ligation of the femoral vein on the amputated side was carried out on 39 patients. The corrected incidence of pulmonary embolism on the 334 patients on whom amputations were carried out without ligation is thus 1.2 per cent, or four times the average for our surgical patients.

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40. Sandblom, P.; Ekström, G., and Quist, O.: Treatment of Local Pyogenic Infections with Heparin, *Acta chir. Scandinav.* **96**:323, 1948.

41. Neuhoof, H., and Seley, G. P.: Acute Suppurative Phlebitis Complicated by Septicemia, *Surgery* **21**:831, 1947.

42. Veal, J. R.: Prevention of Pulmonary Complications Following Thigh Amputation by High Ligation of Femoral Vein, *J. A. M. A.* **121**:240 (Jan. 23) 1943.

Pulmonary embolism occurred after amputation in 4 patients without ligation and in an additional 2 patients after the femoral vein was tied. In neither of the last 2 patients did death result from the pulmonary embolus. Of interest is the fact that both fatal emboli occurring in the unligated group following amputation were accompanied with gas infection of the soft parts of the leg of such extent that ligation was felt inadvisable. Both of these cases occurred before the advent of anticoagulants or present day antibiotics. It is possible that the fatal outcome was assured by the severe toxicity associated with this type of infection.

It now appears that two reasons for failure of this operative procedure as a means of protecting the amputee from embolism are (1) an insufficiently high level of ligation and (2) failure to perform bilateral ligation. Most of the patients in this group were elderly arteriosclerotic patients, many with diabetes. Relief of pain is commonly obtained by these patients by allowing the leg to hang in a dependent position, and many of the patients are necessarily confined to bed for long periods preoperatively, all factors which tend to increase the incidence of thromboembolism.

Since ligation of the inferior vena cava is a hazardous prophylactic measure in these elderly patients, we feel that the incidence of pulmonary embolism can be greatly reduced by ligation of the common femoral vein on the side of amputation and additional ligation of the superficial femoral vein on the opposite side. These measures, carried out at the time of amputation, should offer the best protection to the patient against embolism and result in a minimum of postligation sequelae.

Since the prescribed indications for ligation or anticoagulant therapy often must be adjusted to meet the needs of the patient's disease, instances do exist for the substitution of one form of treatment for another or for their combined use.

#### *Indications for Combined Therapy*

1. Progressive thrombosis or embolism subsequent to one of treatment
2. Necessary interruption of anticoagulant therapy due to
  - a. Hemorrhage
  - b. Intercurrent surgery
  - c. Intercurrent disease in which anticoagulants are undesirable

In chart 6 are listed the complications incident to one or the other form of treatment of thromboembolic disease. In several instances infarction occurred subsequent to the use of the indicated type of vein

ligation or adequate prolongation of the prothrombin time. Likewise, while adequate protection was given against new or repeated pulmonary emboli by venous ligation, progressive or recurrent thrombosis did occur occasionally in the blocked extremity. Such instances afford good reason for the substitution or addition of the other method of treatment. Along with such examples must be mentioned those patients in whom satisfactory progress is occurring with anticoagulant measures but in whom intercurrent operations become suddenly mandatory or a complicating disease becomes apparent toward which anticoagulants would be detrimental. An additional small number of patients in whom individual idiosyncrasies to the anticoagulant drugs are seen must be protected from the fatal sequelae of thromboembolism by venous ligation.

After consideration of the instances in which the use of anticoagulant therapy is ill advised, either in the active management of patients with thromboembolism or as a measure in the prevention of this disease, one must then define the instances for its choice as an effective therapeutic measure. We are of the opinion that the anticoagulants, heparin sodium and dicumarol,<sup>®</sup> are the best means of preventing venous thrombosis and subsequent pulmonary embolism in all patients in whom definite contraindications to their use, as described, do not exist. Similarly, once thromboembolism has occurred, either in the postoperative patient, during enforced rest in bed or immobilization, or in the patient on normal activity, these chemicals when used intelligently and judiciously again afford excellent protection to the patient.

Available for follow-up study more than six months after venous ligation were 99 patients in whom thromboembolism was suspected or apparent (chart 7). Of those having ligations of the common femoral vein 35 per cent had swelling of the entire leg on which the ligation was performed—designated as 3 plus swelling on the accompanying chart. In the same group 24 per cent had swelling of calf and ankle (2 plus) and in 18 per cent the ankle (1 plus) was the only site of swelling. Pain caused some complaint in 41 per cent.

Patients having ligations of the superficial femoral vein had less severe swelling; 19 per cent had 3 plus swelling; 23 per cent had 2 plus swelling, and 26 per cent had ankle edema on the ligated side. Mild discomfort was reported by the same proportion of patients with ligation of the superficial femoral vein as was reported after ligation of the common femoral, but severe pain was present in only 3 per cent.

In the smaller group of patients with ligations of the vena cava, swelling of the entire leg was prominent in only 10 per cent, but 60 per cent of these patients had some swelling of the calf and ankle. None of them experienced disabling discomfort in spite of the swelling.

A similar follow-up study concerned 81 patients with thromboembolism in whom the anticoagulants were employed. The results are

included in chart 8. It is apparent that patients treated with anticoagulants also have post-thrombotic sequelae, although comparison with chart 7 illustrates the decreased frequency of severe swelling and pain when the anticoagulants are used rather than in ligation.

It is certainly not felt that the consideration of post-thrombotic swelling of the leg is the most important factor in the management of

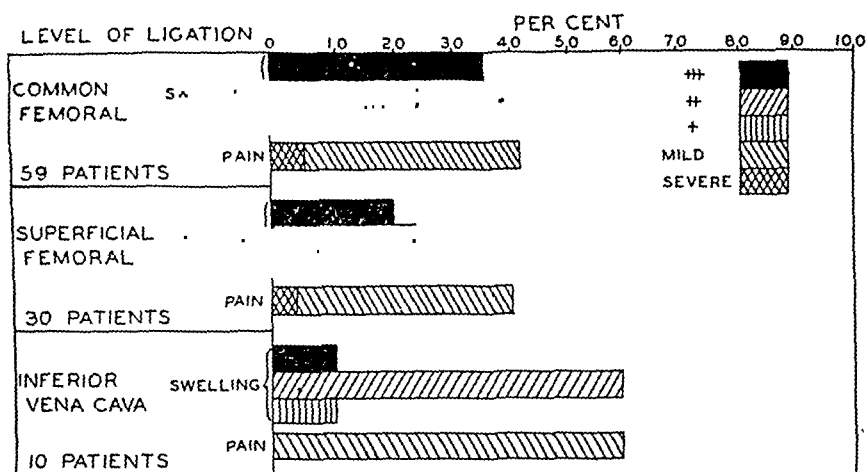


Chart 7.—Complications more than six months after venous ligation.

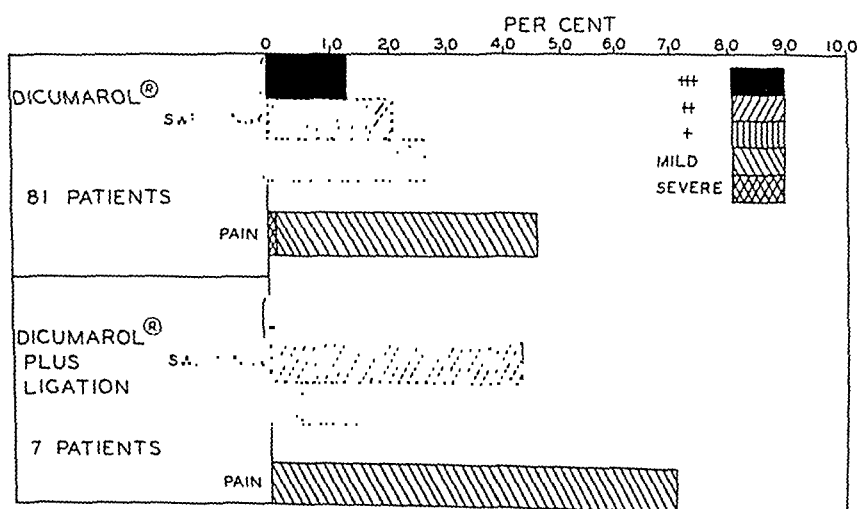


Chart 8.—Complications more than six months after anticoagulant therapy.

thromboembolism. However, we do believe that the administration of anticoagulants, whenever possible, and the use of venous ligation as a supplementary or alternate procedure in the special situations that have been described will result in the greatest protection from embolism with the least delayed discomfort to the patient.

## SUMMARY

1. Experience in the management of thromboembolism at the University Hospital during the past nine years indicates that at present use of anticoagulants is the treatment of choice.
2. The value of interruption of a vein in thromboembolism is apparent in situations in which the anticoagulants are undesirable because of the lack of facilities for their control or of the special risk they represent for certain patients.
3. Anticoagulants and venous ligation have proved effective, in our experience, when employed along with general preventive measures in reducing the incidence of pulmonary embolism.
4. Further reduction in the occurrence of pulmonary embolism may be expected when these procedures are applied early in thromboembolism and when they are extended to the susceptible patient prior to the development of thrombosis or embolism.
5. The sequelae of venous thrombosis were less severe after use of anticoagulants than they were after venous ligation in the patients studied.

# EARLY AND LATE SEQUELAE OF THERAPEUTIC VEIN LIGATION FOR THROMBOSIS OF VEINS OF LOWER LIMBS

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AND

JOSEPH F. ALSOP, M.D.

DETROIT

WHILE excellent results have been reported with the use of both anticoagulant therapy and vein interruption in the treatment of postoperative thromboembolism,<sup>1</sup> a wider experience with their application will have to be gathered before the comparative merits of these two methods can be definitely stated. In any such evaluation the presence,

From the Department of Surgery of the Henry Ford Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

1. (a) Veal, J. R.: High Ligation of the Femoral Vein in Amputations of the Lower Extremities, *J. A. M. A.* **114**:1616 (April 27) 1940. (b) Sears, J. B.: Experience with Femoral-Vein Ligation for Prophylaxis of Postoperative Pulmonary Embolism, *New England J. Med.* **224**:108 (Jan. 16) 1941. (c) Homans, J.: Exploration and Division of the Femoral and Iliac Veins in the Treatment of Thrombophlebitis of the Leg, *ibid.* **224**:179 (Jan. 30) 1941. (d) Welch, C. E., and Faxon, H. H.: Thrombophlebitis and Pulmonary Embolism, *J. A. M. A.* **117**:1502 (Nov. 1) 1941. (e) Lowenberg, E. L.: Femoral Vein Ligation in the Treatment of Pulmonary Embolism Due to Femoral Thrombophlebitis, *Virginia M. Monthly* **71**:288 (June) 1944. (f) Fine, J., and Starr, A.: The Surgical Therapy of Thrombosis of the Deep Veins of the Lower Extremities, *Surgery* **17**:232 (Feb.) 1945. (g) Veal, J. R., and Hussey, H. H.: Surgery of Deep Venous Thrombosis of the Lower Extremity, *ibid.* **17**:218 (Feb.) 1945. (h) O'Neil, E. E.: Ligation of the Inferior Vena Cava in the Prevention and Treatment of Pulmonary Embolism, *New England J. Med.* **232**:641 (May 31) 1945. (i) Gaston, E. A., and Folsom, H.: Ligation of the Inferior Vena Cava for the Prevention of Pulmonary Embolism: A Report of Two Cases, *ibid.* **233**:229 (Aug. 23) 1945. (j) Pratt, G. H.: Surgical Management of Thrombosis and Thrombophlebitis with Discussion of Vein Resection, *New York State J. Med.* **46**:1825 (Aug. 15) 1946. (k) Homans, J.: Medical Progress: Diseases of Veins, *New England J. Med.* **235**:163 (Aug. 1) 1946. (l) Moses, W. R.: Ligation of the Inferior Vena Cava or Iliac Veins, *ibid.* **235**:1 (July 4) 1946. (m) Hershey, C. D., and Bailey, R. B.: Vein Ligation in Thrombophlebitis, *South. M. J.* **39**:804 (Oct.) 1946. (n) Allen, A. W.: Interruption of the Deep Veins of the Lower Extremities in the Prevention and Treatment of Thrombosis and Embolism, *Surg., Gynec. & Obst.* **84**:519 (April) 1947. (o) Veal, J. R.; Hussey, H. H., and Barnes, E.: Ligation of the Inferior Vena Cava in Thrombosis of the Deep Veins of the Lower Extremities, *ibid.* **84**:

(Footnote continued on next page)



extent and permanence of the early and late sequelae associated with each method will have to be carefully weighed.

As regards vein interruption, in spite of a rather large number of published accounts dealing with its use, accurate data on postligation complications and residuals are scarce.<sup>2</sup> A follow-up survey of even a relatively small series of cases would, therefore, seem useful. Such a survey forms the main subject of this study. In addition to an analysis

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605 (April 15) 1947. (*p*) Donaldson, G. A.: The Therapy and Prophylaxis of Venous Thrombosis and Pulmonary Embolism, *Surg. Clin. North America* **27**: 1037 (Oct.) 1947. (*q*) Linton, R. R., and Hardy, I. B.: Postthrombotic Sequelae of the Lower Extremity: Treatment by Superficial Femoral Vein Interruption and Stripping of the Saphenous Veins, *ibid.* **27**:1171 (Oct.) 1947. (*r*) Homans, J.: Venous Thrombosis and Pulmonary Embolism, *New England J. Med.* **236**:196 (Feb. 6) 1947. (*s*) Pratt, G. H.: Surgical Management of Venous Clotting, *S. Clin. North America* **28**:341 (April) 1948. (*t*) McClure, R. D., and Lam, C. R.: Experiences in Heparin Administration, *J. A. M. A.* **114**:2085 (May 25) 1940. (*u*) Lam, C. R.: Heparin Administration: Methods and Results in Thirty Cases, *Am. Surg.* **114**:205 (Aug.) 1941. (*v*) Bauer, G.: Venous Thrombosis, *Arch. Surg.* **43**: 462 (Sept.) 1941. (*w*) Jorpes, E.: Pure Heparin for the Prevention and Treatment of Thrombosis, *Acta med. Scandinav.* **107**:107, 1941. (*x*) Wetterdall, P.: The Use of Heparin as a Prophylactic against Thrombosis Following Gynecologic Operations, *ibid.* **107**:122, 1941. (*y*) Crafoord, C.: Heparin as a Prophylactic Against Postoperative Thrombosis, *ibid.* **107**:116, 1941. (*z*) Bauer, G.: Heparin and Venous Thrombosis, *J. A. M. A.* **131**:196 (May 18) 1946. (*a'*) Ziliacus, H.: The Results of Five Years' Treatment of Thrombosis and Pulmonary Embolism at a Series of Swedish Hospitals During the Years 1945 to 1946, *Acta med. Scandinav. (supp.)* **171**:1, 1946. (*b'*) Jorpes, E.: Anticoagulant Therapy in Thrombosis, *Surg., Gynec. & Obst.* **84**:677 (April 15) 1947. (*c'*) Murray, G.: Anticoagulants in Venous Thrombosis and the Prevention of Pulmonary Embolism, *ibid.* **84**:665 (April) 1947. (*d'*) Evans, J. A., and Boller, R. J.: The Prevention of Postoperative Pulmonary Embolism, *New England J. Med.* **236**:392 (March 13) 1947. (*e'*) Cosgriff, S. W.; Cross, R. J., and Habif, D. V.: The Management of Venous Thrombosis and Pulmonary Embolism, *S. Clin. North America* **29**:324 (April) 1948. (*f'*) Barker, N. W.; Cromer, H. E.; Hurn, M., and Waugh, J. M.: The Use of Dicumarol in the Prevention of Postoperative Thrombosis and Embolism with Special Reference to Dosage and Safe Administration, *Surgery* **17**:207 (Feb.) 1945. (*g'*) Deleted on proof. (*h'*) Smith, G. V. S., and Milligan, W. J.: Dicumarol Prophylaxis Against Venous Thrombosis in Women Undergoing Surgery, *Surg., Gynec. & Obst.* **86**:461 (April) 1948. (*i'*) Shlevin, E. L., and Lederer, M.: Uncontrollable Hemorrhage after Dicoumarol Therapy with Autopsy Findings, *Ann. Int. Med.* **21**:332 (Aug.) 1944. (*j'*) Loewe, L.; Hirsch, E.; Grayzel, D. M., and Kashdan, F.: The Action of Heparin in Experimental Venous Thrombosis, *Surgery* **22**:746 (Nov.) 1947. (*k'*) Kiesewetter, W. B., and Shumacker, H. B. Jr.: An Experimental Study of the Comparative Efficacy of Heparin and Dicumarol in the Prevention of Arterial and Venous Thrombosis, *Surg., Gynec. & Obst.* **86**:687 (June) 1948.

2. Northway, R. O., and Buxton, R. W.: Ligation of the Inferior Vena Cava, *Surgery* **18**:85 (July) 1945. Ray, C. T., and Burch, G.: Vascular Responses in Man to Ligation of the Vena Cava, *Arch. Int. Med.* **80**:587 (Nov.) 1947.



It is significant that in 43 per cent of the cases the presenting sign or symptom was that of pulmonary embolism and that in 5 per cent more it consisted in advanced involvement of the limbs in the form of tenderness of the thigh (2 per cent) and edema of the leg (3 per cent) (table 4). These findings, together with the distribution of the signs and symptoms of the fully developed clinical picture (that includes an incidence of 55 per cent of embolic phenomena and of 23 per cent of

TABLE 3.—*Age and Sex Incidence*

Age, Years	Patients, Number	
21-30.....	7	
31-40.....	16	Average age: 51 yrs.
41-50.....	20	
51-60.....	27	(b) Males — 63 patients
61-70.....	19	
71 .....	11	Females — 37 patients
Total.....	100	

TABLE 4.—*Distribution of Presenting Symptoms or Signs*

Symptom or Sign	Number of Cases
Calf, pain or tenderness.....	57
Chest { pain.....	5 }
{ signs.....	38 }
Leg, swelling.....	3
Thigh, pain or tenderness.....	2

TABLE 5.—*Distribution of Symptoms and Signs in the Established Clinical Picture*

Symptom or Sign	Number of Cases
Calf, pain or tenderness.....	88
Chest, pain or signs.....	52
Thigh, pain or tenderness.....	23
Hemoptysis .....	26

involvement of the thigh) (tables 5 and 6), indicate that in a high proportion of the patients treated the thromboembolic process was well advanced.

Table 6 merits comment on account of its negative qualities. The large number of incomplete examinations of the limbs speaks ill for the thoroughness of the house staff. It should be added, however, that most of the insufficient information dates from the first four years of the survey, when the present concept of the elusiveness of the clinical picture of thromboembolic disease had not yet become general knowledge.

In the latter years the attitude of uncompromising suspicion has been accepted by most of the staff of this hospital, and the examinations of the limbs have become frequent and painstaking.

An analysis of the evidence of pulmonary embolism (table 7) brings out a point that always bears stressing: Pulmonary embolism in a varying number of cases cannot be verified roentgenologically.

The meaning of table 8, showing the incidence of elevated temperature and pulse rate, is not entirely clear. While the lingering of postoperative fever and tachycardia or the appearance of an elevated temperature and

TABLE 6.—*Local Signs and Extent of Involvement*

A. Local Signs of Involvement of Veins			
	Present	Absent	Not Stated
Tenderness in calf.....	88	12	..
Tenderness in thigh.....	23	20	57
Plantar tenderness.....	6	12	82
Homans' sign.....	52	7	41
Edema .....	21	11	68
B. Extent of Clinical Involvement of Veins			No. of Cases
Calf .....			102
Calf and thigh.....			22
Thigh only.....			2
None .....			24

TABLE 7.—*Incidence of Pulmonary Embolism*

	Number of Cases
A. Total Incidence .....	55
B. Evidence of Pulmonary Infarction	
Clinical signs and .....	55
Roentgenographic .....	40
C. Signs and Symptoms of Pulmonary Embolism	
Pain in chest.....	52
Signs in chest.....	43
Hemoptysis .....	26

pulse after a normal period, in general, are strong warnings of the possibility of venous thrombosis, in any individual case the persistence of the postoperative rise may be difficult to interpret. It seems undeniably important, however, that in 74 and 71 per cent of the cases studied the temperature and pulse rate, respectively, were above normal.

There is evidence<sup>1b</sup> that early postoperative rising reduces the incidence of postoperative venous clotting. That phlebothrombosis may occur in spite of early ambulation is also generally accepted. In this short series, in 11 patients out of 77 who were up and about on the day of their operation venous clotting developed; on the other hand, over half (50.7 per cent) of the patients had been kept in bed for over seven days postoperatively.

In view of the purpose of this study, the data contained in table 9 have special significance. There is ample proof that the time of inception of the treatment in relation to the time of onset of the symptoms of venous thrombosis has much bearing on the results of treatment with anticoagulants<sup>3</sup>; the earlier the diagnosis and the prompter the treatment, the better are the results, both as to local residuals and as to prevention of embolism. It is reasonable to assume that this is probably true also in regard to treatment with vein interruption. Thus it is meaningful that the lapse of time between the appearance of the first symptom or sign and the time of treatment in this series (table 9) averaged six days after operation and eighteen days when operation was not performed.

TABLE 8.—*Pulse Rate and Temperature*

	Number of Cases
A. Temperature	
99 — 100 F.....	19
100 plus F.....	55
B. Pulse	
10 — 100 min.....	29
100 plus min.....	42

TABLE 9.—*Interval Between Time of First Symptom or Sign of Venous Thrombosis and Time of Ligation*

Interval, Days	Number of Cases
Less than 1.....	19
1-2.....	27
3-7.....	22
8-14.....	17
15-28.....	12
Over 28.....	3

Several factors contributed to the delay in the institution of treatment. In the medical cases throughout the entire period surveyed the tendency has been to try conservative management first and to resort to surgical treatment only if the course was not favorably influenced. As regards postoperative venous thrombosis, the same point of view prevailed in some of the earlier cases, whereas in many others (in the first years of the period covered) diagnosis was not conclusively made until advanced signs appeared. In the surgical services, during the last four years the outlook has radically changed and no time is lost before starting the treatment. Nevertheless, the length of the "waiting time" for the entire group of cases remains excessively high. This fact, together

3. Bauer,<sup>1v,z</sup> Jorpes.<sup>1b'</sup>

with the other evidence, already given, of the advanced character of a large portion of these cases, must be borne in mind when judgment is made of the postligation sequelae.

*Types of Vein Interruption.*—In the 100 cases 146 procedures of vein interruption were carried out. The classification of these operations is shown in table 10. All but 5 of the procedures were ligations in continuity. In 2 of the early cases the vein (in both cases the common femoral) was opened and the clot, as far as possible, removed. In 3 instances the vein (the common femoral) was opened in order to ascertain the absence or presence of clotting at the exposed level, and, a thrombus not having been found, the vein was tied. Early we reached the decision that removal of the clot was not a reliable procedure, chiefly because of the probability of the reformation of the clot in the vein segment whose intima had been damaged at the site of thrombosis and further insulted by the operative intervention. Concerning the site of ligation, in the earlier

TABLE 10.—*Classification of Operations*

A. Type of Operation	Number of Cases
Ligation in continuity.....	141
Section and ligation.....	3
Thrombectomy and ligation.....	2
B. Level of ligation (number of cases)	
Unilateral	
Left superficial femoral.....	21
Right superficial femoral.....	20
Left common femoral.....	3
Right common femoral.....	4
Left common iliac.....	1
Right common iliac.....	1
Bilateral	
Superficial femoral.....	41
Common femoral.....	2
Left common femoral with right superficial femoral.....	2
Left common iliac with right superficial femoral.....	1
Vena cava ligation.....	4

cases much experimentation had to be done. Eventually the following principles of conduct were accepted.

If the clinical involvement is limited to the popliteal vein or to levels below, the common femoral vein is exposed through a subinguinal incision. (The incision is usually parallel to the inguinal crease, being placed 2 cm. distal to it and centered on the femoral pulsation. However, a good many longitudinal incisions were also employed. Provided care is taken not to injure the subinguinal lymphatic nodes there seems to be little to choose between the two types of approach; wounds made in either way healed without a single important complication.) During the exposure and dissection, the greater saphenous vein is used as a guide to the femoral sheath and its branches are carefully saved. Enough of the femoral trunk is brought into view to determine the site of embouchure of the deep femoral vein or one of the deep circumflex femoral veins. Our impression at the operating table, confirmed by anatomic studies of others,<sup>4</sup> has been that the topographic disposition of the deep femoral vein is quite variable and that often it joins the superficial femoral vein at levels so low

4. Edwards, E. A., and Robuck, J. D., Jr.: Applied Anatomy of the Femoral Vein and its Tributaries, Surg., Gynec. & Obst. 85:547 (Nov.) 1947.

that its operative visualization entails a forbidding amount of dissection. Therefore, if along an 8 or 10 cm. segment of the main femoral trunk a definite vena profunda femoris is not found, a circumflex vein (either medial or lateral) not less than 1 cm. in diameter is selected as the site of ligation. An operative detail of utmost importance is the placing of the ligature distal but as close to such a branch as possible without encroaching on its lumen. In this manner one probably prevents the formation of a stagnant column of blood in the segment of vein directly proximal to the ligature. Operations done in this manner have been listed by us as ligations of the superficial femoral vein, although in a small number of cases the level of ligation may, in fact, have been proximal to the profunda femoris branch. Clinically the difference cannot be detected.

The material used for ligation has been 00 (U. S. P.) braided silk; two ligatures are placed 0.5 cm. apart. The placing of the ligature is always preceded by a careful inspection and palpation of the exposed segment of the vein. We believe that it is possible to determine the absence of clotting in the vast majority of cases. If there is any doubt, the venous trunk is opened. If there is thrombosis but a segment of the common femoral trunk distal to the greater saphenous vein is free from it, the ligation is carried out at that level. If the thrombosis has extended to a level proximal to the saphenofemoral junction, ligation below the inguinal ligament is thought ill advised.

Whenever there is a choice, therefore, we favor ligation of the superficial femoral vein in the sense just mentioned. Ligation of the common femoral vein is reserved for cases of thrombosis extending proximal to the highest circumflex branch but leaving the saphenofemoral junction free. In clinical practice the uppermost limit of thrombosis is difficult to determine and the decision whether to use one or the other level is usually made at the operating table. After several femoral explorations, we have learned that when the clinical evidence of thrombosis suggests involvement of the common femoral vein, it is wiser to ligate above the external iliac level. When this circumstance occurs on one side, with the other side entirely uninvolved, it constitutes our only indication for ligation of the common iliac vein.<sup>5</sup> If the condition is present bilaterally, ligation of the vena cava is the procedure of choice. Aside from using it in cases of bilateral involvement of the entire femoral venous system, we have resorted to ligation of the vena cava also in cases with definite evidence of pelvic venous thrombosis.

In the earlier cases of the series, interruption of the vein was limited to the extremity that was clinically judged to be involved. Increasing experience both in our hospital and elsewhere soon taught us that unilateral ligation carries an appreciable risk, even if the opposite limb is watched with especial care. Examples of instances in which unilateral ligation proved dangerously inadequate will be given subsequently. At present, bilateral ligation is performed in every case, regardless of the limitation of clinically evident signs to one side.

*Anticoagulant Therapy and Vein Ligation.*—There is no *a priori* reason for opposing anticoagulant therapy as a measure adjuvant to vein interruption. We have attempted, however, to rely on vein ligation alone as often as practicable in order to be better able to evaluate its worth. In a few cases resort had to be made to the use of anticoagulant drugs to treat embolic complications following ligation; these cases will

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5. Such an operation is always accompanied with a prophylactic contralateral ligation of the superficial femoral vein.

be discussed presently. In 7 cases heparin and in 1 case dicumarol,<sup>®</sup> in full therapeutic doses, either failed to prevent embolism or caused serious complications and had to be supplanted by ligation. In a number of instances, and mainly in other services, anticoagulant drugs were administered in nontherapeutic doses in conjunction with ligation, for questionable reasons (table 11). Since the postoperative dosage in these cases was not fully therapeutic, the effect of the drugs on the ultimate results of vein ligation may be disregarded. A separation of the cases in which some partial effect may have been brought about is impossible for practical reasons.

### RESULTS

The therapeutic results of vein interruption can be evaluated from two points of view: that of its success in preventing pulmonary embolism and that of its effect on the subsequent evolution of the local thrombotic process.

*Prevention of Pulmonary Embolism.*—Taking all cases, 8 operations were followed by pulmonary embolic episodes (table 12). A brief

TABLE 11.—*Anticoagulant Drugs and Ligation*

	Number of Cases
A. Anticoagulant drugs used	
Because of failure of ligation.....	1
To complement ligation.....	20*
B. Ligation done because of failure of anticoagulants.....	7

\* Nontherapeutic doses administered in 18 cases.

review of these cases is instructive. In the first 5 cases unilateral ligation was done; in the last 3, bilateral ligation.

CASE 1.—M. B. had traumatic thrombophlebitis of the left leg, followed by pulmonary embolism one month later. Ligation of the right superficial femoral vein was done on April 6, 1943. One month later (while bedfast) the patient had another pulmonary infarct, and dicumarol<sup>®</sup> therapy was instituted. The patient recovered.

CASE 2.—J. A. had primary phlebothrombosis of the right leg with pulmonary infarct treated for three weeks as pneumonia. On Jan. 30, 1944 signs of phlebothrombosis of the right common femoral vein appeared. The right common iliac vein was ligated immediately. Another pulmonary infarct occurred on February 5 and was followed by ligation of the left superficial femoral vein. Recovery was uneventful.

CASE 3.—J. M. underwent complete hysterectomy on May 1, 1944. On the fourteenth postoperative day pulmonary embolism with mild signs of phlebothrombosis in the left leg developed. The left superficial femoral vein was ligated on May 17 and the patient was discharged improved. On readmission, July 1, there were evidence of pulmonary embolism and a slight clinical suggestion of phlebothrombosis in the right leg. The right superficial femoral vein was immediately ligated and the patient recovered.



CASE 4.—C. R., with primary thrombophlebitis of the right leg, underwent ligation of the right superficial femoral vein on Aug. 23, 1946. Pulmonary embolism occurred on September 6. Ligation of the left superficial femoral vein was done immediately. The patient recovered.

CASE 5.—A. C., with rheumatic heart disease with congestive failure and auricular fibrillation, was admitted to the hospital after repeated episodes of pulmonary embolism. On the indication of tenderness in the right calf, the right superficial femoral vein was ligated on Aug. 23, 1946. The patient was discharged improved but six weeks later was readmitted with signs of new pulmonary infarct. Death occurred on the day of admission before treatment could be given. Autopsy was not done.

CASE 6.—A. S., who had rheumatic heart disease with congestive failure and auricular fibrillation, was admitted with recent pulmonary infarct and questionable clinical signs of phlebothrombosis in the right calf. Bilateral ligation of the superficial femoral vein was done on Oct. 15, 1946. The patient died suddenly of pulmonary embolism seven days later. At autopsy many pulmonary infarcts of various ages were observed. The source of the embolism was not found (probably the heart; the legs were not dissected out, but the pelvic veins were normal).

TABLE 12.—*Pulmonary Embolism After Ligation*

	Number of Cases
Embolism following unilateral operation.....	5*
Treated with anticoagulant drug.....	1
Treated with ligation.....	3
Embolism following bilateral operation.....	3*
Treated with anticoagulant drug.....	2
Nonfatal embolism attributable to failure of ligation.....	1
Fatal embolism attributable to failure of ligation.....	0

\* Treatment not administered in 1 case.

CASE 7.—F. B., with sickle cell anemia with hemolytic crises, underwent splenectomy on June 13, 1947. Signs of pulmonary embolism were noted on the sixth postoperative day without definite localization of the source of the embolism. Six days later bilateral ligation of the superficial femoral vein was done. Three days later another pulmonary embolism occurred. Heparin and dicumarol® therapy was begun, and the patient recovered.

CASE 8.—H. N. underwent gastroenterostomy with bilateral subdiaphragmatic vagal neurectomy on Nov. 1, 1947. Evidences of phlebothrombosis involving the right common femoral vein were noted one week later. The right common iliac vein was ligated immediately. The patient was discharged improved and made uneventful progress for eleven and a half months postoperatively, when (while the patient was at home out of town) pain in the left leg appeared. On return to the hospital on Nov. 20, 1948 there was clinical but no roentgenologic evidence of pulmonary embolism. Ligation of the left superficial femoral vein was done immediately. The patient was discharged improved, but three weeks after the second ligation a massive pulmonary embolus occurred while the patient was at home (out of town). Treatment with heparin was followed by recovery.

In how many of these cases may one rightfully ascribe the failure to prevent embolism to the inherent shortcomings of ligation as a method of treatment?

The first step in looking for an answer must be the examination of the indications for the use of vein interruption in each case. It is readily seen that in cases 5, 6 and 7 the source of embolism was not clear. In cases 5 and 6 (both cases of rheumatic heart disease with congestive failure) in particular there was little justification for expecting any benefit from vein ligation; as the final outcome strongly suggests, both these patients had emboli from the right side of the heart.

The next point of inquiry concerns the question whether, if ligation was indicated, the correct procedure was chosen. In this respect it is noted that, leaving case 8 aside as a special problem to be discussed presently, in all the remaining cases ligation was unilateral and that in all these cases in which a second ligation was resorted to the embolic episodes were satisfactorily controlled. This fact would therefore suggest that the failure of the first ligation was due to the incompleteness of the procedure for the given situation rather than to any immanent fault of the method.

The last case (case 8) is difficult to analyze. The first operation (ligation of the right common iliac vein) apparently was adequate to treat the thrombosis, for the patient progressed very well for almost a year. The second ligation (of the left superficial femoral vein) again seemed sufficiently radical, since no thrombosis of the common femoral vein was found on exploration. When the latter procedure was followed in a week by a grave episode of pulmonary embolism, we assumed that a clot must have formed proximal to the point of ligation and broken away. This assumption was proved incorrect, however, when, two months after the last embolic incident, phlebograms showed the left common femoral vein to be well filled. It must be further theorized that this patient has had—perhaps still has—a nidus of thrombosis outside the principal venous trunks draining the limbs, possibly in the pelvis.

In summary, therefore, one can state that vein interruption affords a very high degree of safety for the prevention of the embolic complications of thrombosis, provided the operative indications are correct, the level of the ligation high enough and the operation bilateral. Excluding the instances of inadequate operation (4 cases) and grossly erroneous choice of methods (3 cases), we encountered only 1 case (case 8) in which interruption of the vein above the level of thrombosis failed to give full protection against embolism.

*Effect on the Local Pathologic Process.*—The second aspect of the analysis of the results of vein interruption is concerned with the effects of the procedure on the local thrombotic process. This phase of the inquiry can be conveniently divided into the examination of the immediate results and that of the late sequelae.

Early Effects: In table 13 are listed the observations made on the appearance of (if none was previously present) or increase in the swelling of the limbs after ligation. These data are either translations of actual preligation and postligation measurements of the extremities or interpretations of the progress notes on the records. It is evident that swelling occurs in at least 80 per cent of the limbs operated on. Clinically the swelling appears to have two components: venous congestion and interstitial exudation (edema). At times the swelling is associated with aching pain and tenderness; at others, it is entirely symptomless.

The opinion is generally held that the swelling is commoner and more pronounced in cases in which the extent of the thrombosis already established at the time of ligation is greater. This is our impression also, although our statistical data are not entirely convincing on this point. It would be wrong, however, to interpret this fact as proof (as

TABLE 13.—*Incidence of Early Postligation Swelling of the Limb*

Degree of Swelling	Number of Limbs	Percentage of Total
None.....	10	7
Slight.....	48	32
Moderate.....	62	41
Severe.....	10	7
Not stated.....	20	13

has been done by some) that the degree of postligation swelling is determined solely by the degree of preexisting thrombosis. Obviously, an increase in the swelling (or the appearance of swelling) can be postulated to take place either if there is no extension of thrombosis after ligation but by the ligation certain important drainage channels are shut off, or if after ligation the thrombotic process grows more extensive and, in addition to the surgical blocking of the venous return, it further reduces the available return pathways. Which of these two possibilities or what combination of them actually happens in a given case is impossible to say at present. We attempted a statistical evaluation of our cases in this respect, but our data are insufficient to allow any conclusion. Indeed, even a very large number of cases, with accurate and frequent measurements of limbs, would probably be of doubtful value for answering the question. Evidently methods other than clinical observation and measurement must be resorted to. In paragraphs to follow a brief account will be given of our experience with phlebography which has given promise of elucidating at least some phases of this problem.

The question of postoperative swelling has, of course, more than theoretic interest. As the precursor of the late sequelae, it must be taken into serious account whenever the advantages and disadvantages of vein ligation are weighed.

Late Sequelae: We attempt to follow our patients with vein ligation indefinitely in the clinic. It has been possible to maintain contact until the present with well over half of the patients. Over 20 per cent more were repeatedly examined in the past for periods of three months to three years after their operations before they either died or dropped out of sight. Seven patients have kept us up to date on their condition by correspondence. Thus we have satisfactory records of progress for

TABLE 14.—*Success of Follow-Up*

Method of Follow-Up	Number of Cases*
Current clinic visits.....	66
Current correspondence.....	7
Clinic visits in the past (3 mo. to 3 yr.).....	23
None .....	4

\* Fifteen patients are dead of causes unrelated to the operation on the vein.

TABLE 15.—*Length of Follow-Up*

Length of Follow-Up, Years	Percentage of Total Cases Followed
1/12-1/2.....	15.5
7/12-1.....	8.7
2-3.....	50.0
4-5.....	20.1
6-7.....	5.2

\* Four cases (4 per cent of total) were lost from observation.

a year or more in 76 per cent of the cases in which we operated. In tables 14 and 15 are listed the details of the extent and length of the follow-up.

The establishment of objective, or at least reliable, criteria for the appraisal of the functional condition of a formerly diseased limb is a very difficult task. We chose for our follow-up examinations the following graded functional classification: "Sequelae absent": no swelling at rest or exercise; no complaint for which objective explanation can be found; physical condition of the limb normal; measurements (circumference of the ankle just above the inner malleolus, of the calf at its largest girth and of the thigh 20 cm. above the upper border of the patella) normal. "Sequelae slight": no swelling at rest, slight swelling on exercise; no complaint (as in preceding classi-

fication); physical condition of the limb normal at rest, with slight edema on exercise; measurements normal. "Sequelae moderate": slight edema at all times, made worse by exercise; bandage or elastic hose worn; complaint of aching fulness of moderate degree on exercise; slight degree of varices, induration or edema of the leg; measurements no more than 2 cm. above those normal for the patient (when these are known). "Sequelae severe": definite edema at rest, much aggravated by exercise, and use of a bandage or elastic hose obligatory; complaint of severe aching, fulness or claudication; prominent varices, pronounced induration, static dermatitis or ulceration; measurements more than 2 cm. above normal.

While these categories of classification are arbitrary, the criteria on which they are based were applied as uniformly and objectively as the nature of the investigation permitted.

Table 16 summarizes the findings in the limbs when last seen.

TABLE 16.—*Late Sequelae of Vein Ligation*

Classification of Sequelae	Number of Limbs	Percentage of Total
Absent.....	50	33
Slight.....	52	35
Moderate.....	39	26
Severe.....	2	1
No follow-up.....	7	5

Before we attempt a comprehensive appraisal of the results, some remarks on observations made during the follow-up periods seem to be in order.

When watching the progress of these patients one is soon impressed with the importance of the attention the patient is willing or able to apply to the care of the limbs. Simple measures of physical therapy (massage and exercises), the conscientious use of elastic bandages or hose whenever swelling appears, prompt treatment of cutaneous lesions and avoidance of trauma of any kind contribute remarkably to the rehabilitation of the extremity. Restitution to normal of some of the limbs that were extensively involved at the time of ligation often has been surprisingly complete. On the other hand, in several of the cases with more pronounced sequelae the functional impairment of the leg was due not so much to the ravages of venous thrombosis as to the neglect in the care of the limbs. One of the patients classified as having sequelae of severe degree and who has a static ulcer is entirely remiss in attending to the care of his leg.

Every limb followed showed progressive improvement after the first month after ligation, provided the necessary minimum care was

taken by the patient. Clinically at least, the formation of collaterals appears to be well advanced by this time in the majority of cases. Improvement may go ahead for as long as a year, after which little change for the better is noted. Seemingly the hemodynamic adjustments reach their peak at the end of this period.

A special word may be said regarding the cases of ligation of the vena cava. Two of the patients have moderate and 2 slight residuals; all 4 continue their previous occupations (they are all housewives) without serious handicap other than the demands of the special care of their limbs. All 4 originally had very extensive pelvic thromboses with sublethal pulmonary emboli.

The current concepts of the mechanism of physiologic restitution after phlebothrombosis have been repeatedly described,<sup>6</sup> and our clinical studies can add to them nothing new. (Some observations made in studying the phlebographic appearances of these limbs will be described in subsequent paragraphs.)

TABLE 17.—*Relationship of Preligation Involvement to Late Sequelae*

N. B. 120 limbs evaluated	Extent of Involvement	Number of Limbs	Incidence of Late Sequelae, Percentage of Total			
			None	Slight	Moderate	Severe
	None.....	20	50	19	31	0
	Calf.....	79	28	40	32	0
	Thigh.....	20	24	33	33	10

The relationship of the degree of preligation thrombosis to the severity of early swelling after vein interruption has been mentioned. In table 17 the grouping of late sequelae in relation to the original degree of vein involvement, as judged clinically, is given. While the number of cases is too small to allow valid statistical conclusions, the trend of evidence seems to confirm the assumption that the more extensive the thrombotic process the severer are the sequelae.

Since there is available no like series of cases of venous thrombosis treated with anticoagulants or with the methods (largely useless) popular before the advent of anticoagulants or vein interruption, a comparative appraisal of the results is not possible. Without any claim to superiority for the method, it can be said, however, that in this group of ligations, comprising a high proportion of operations for advanced venous thrombosis, the condition of a third of the limbs has returned to normal, that the condition of another third has improved enough to

6. Veal, J. R., and Hussey, H. H.: The Pathologic Physiology of the Circulation in Acute, Thrombophlebitis and the Postthrombotic Syndrome, *Am. Heart J.* 23:390 (March) 1942. Bauer.<sup>17</sup>

be no more than a slight inconvenience to the patient and that even in the least satisfactory cases it has not interfered with the pursuit of a normal and useful life.

#### PHLEBOGRAPHY

As mentioned earlier, the evolution of the process of clotting in the veins of the limb after ligation is impossible to follow accurately by purely clinical means. The visualization of the venous system of the lower extremity with the help of a radiopaque dye seemed to us to offer a more promising method for this purpose.

*Technic of Phlebography.*—We have used phlebography in the past sporadically as a diagnostic aid in venous thrombosis with rather indifferent results. Our impression had been that in the conventional technics<sup>7</sup> a number of factors that determine the passage of the dye into the deep veins of the leg and thence into the venous system of the thigh are uncontrolled. Thus parts of the deep system may remain unfilled by the dye and may be wrongly interpreted as pathologically obstructed. In our inquiry there was also another technical difficulty to overcome: the simultaneous complete visualization of the venous systems of both the leg and the thigh. In the technics formerly described, because of the smallness of the quantity of dye introduced

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7. Franklin, K. J.: A Monograph on Veins, Springfield, Ill., Charles C Thomas, Publisher, 1947. Bauer, G.: Venographic Studies of Thromboembolic Disease, *Acta chir. Scandinav.* (supp. 61) **84**:1, 1940. Starr, A.; Frank, H. A., and Fine, J.: The Venographic Diagnosis of Thrombophlebitis of the Lower Extremities, *J. A. M. A.* **118**:1192 (April 4) 1942. Welch, C. E.; Faxon, H. H., and McGahey: The Application of Phlebography to the Therapy of Thrombosis and Embolism, *Surgery* **12**:163 (Aug.) 1942. Luke, J. C.: Retrograde Venography of Deep Leg Veins, *Canad. M. A. J.* **49**:86 (Aug.) 1943. Baker, E. C., and Sedwitz, S. H.: Observations on Venography of the Lower Extremities, *Radiology* **41**:451 (Nov.) 1943. DeBakey, M. E.; Schroeder, G. F., and Ochsner, A.: Significance of Phlebography in Phlebothrombosis, *J. A. M. A.* **123**:738 (Nov. 20) 1943. Baker, E. C., and Miller, F. A.: Further Experiences with Venography, *Radiology*, **43**:129 (Aug.) 1944. Papper, E. M., and Imler, A. E.: Use of Phlebography and Lumbar Sympathetic Block in the Diagnosis of Venospasm of the Lower Extremity, *ibid.* **15**:402 (March) 1944. Lesser, A., and Danelius, G.: Venography: Its Value in the Diagnosis and Management of Venous Disturbances of the Lower Extremities, *Ann. Surg.* **119**:903 (June) 1944. Oliver, C.: Phlébographie et phlébectomie dans les phlébitis postopératoires récentes et profondes du membre inférieur, *Presse méd.* **53**:132 (March 17) 1945. Farinas, P. L.: Abdominal Venography, *Am. J. Roentgenol.* **58**:599 (Nov.) 1947. O'Laughlin, B. J.: Roentgen Visualization of the Inferior Vena Cava, *ibid.* **58**:617 (Nov.) 1947. Bull, D. C.: Phlebography of Lower Extremity, *S. Clin. North America* **28**:541 (April) 1948. Allen, E. G.; Hines, E. A., Jr.; Walter, P. O.; Kayle, F., and Barker, N. W.: The Use of Dicumarol as Anti-Coagulant: Experience in 2307 Cases, *Ann. Int. Med.* **27**:37 (Sept.) 1947.

and also because of the way of introduction, the veins of the thigh and lower part of the pelvis are seldom filled (even if the veins of the legs are well outlined); the dye is usually too diluted when it reaches the upper segments of the venous system of the thigh to give a sharp shadow.

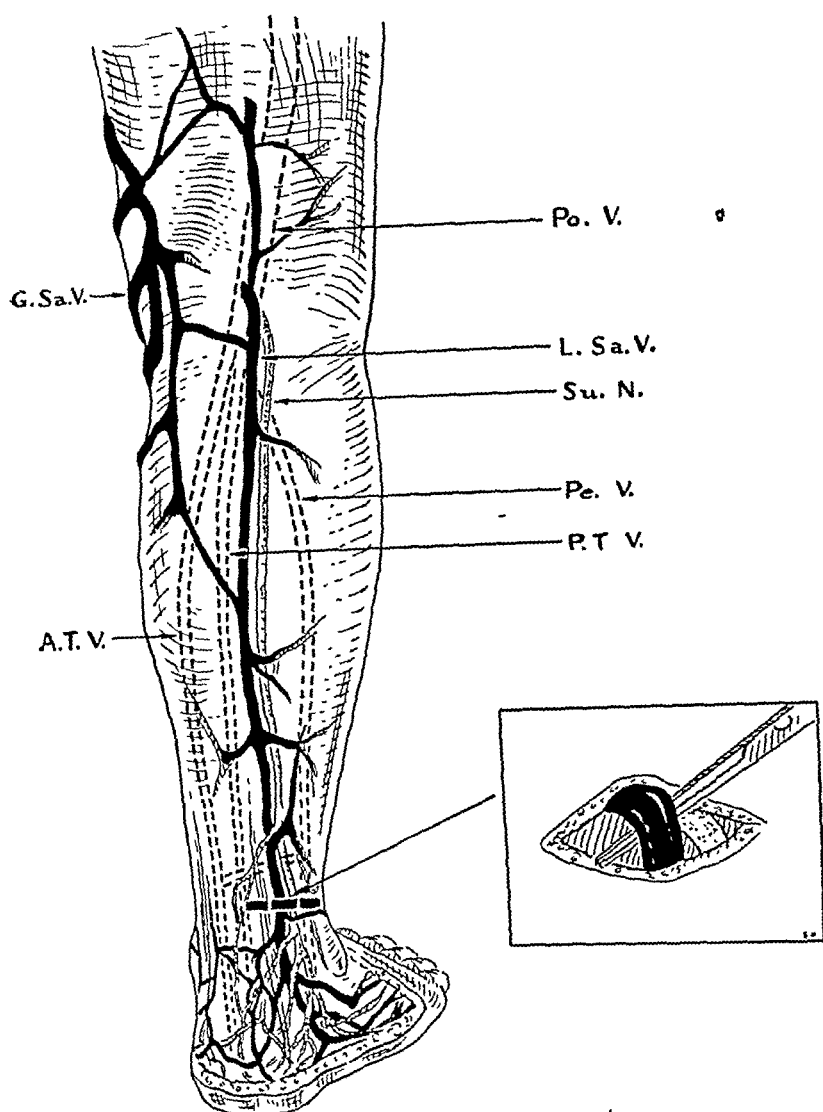


Fig. 1.—Sketch of the right leg showing the relationships of the lesser saphenous vein to the popliteal vein and sural nerve. The site of incision is marked with heavy broken lines running from the lateral malleolus to the border of the achilles tendon. *Po.V.* indicates the popliteal vein; *G.Sa.V.*, the greater saphenous vein; *L.Sa.V.*, the lesser saphenous vein; *Su.N.*, the sural nerve; *Pe.V.*, the peroneal vein; *P.T.V.*, the posterior tibial vein; *A.T.V.*, the anterior tibial vein.

After numerous trials with modifications of earlier technics, the following procedure was worked out (figs. 1 and 2).



With the patient prone, a 1 cm. long incision is made over the lesser saphenous vein slightly proximal to the point where it is formed by its tributaries from the foot. The location of the incision is shown in figure 1. If a transverse line is drawn from the upper border of the malleolar prominence of the fibula to the lateral border of the achilles tendon and this line is divided into three equal

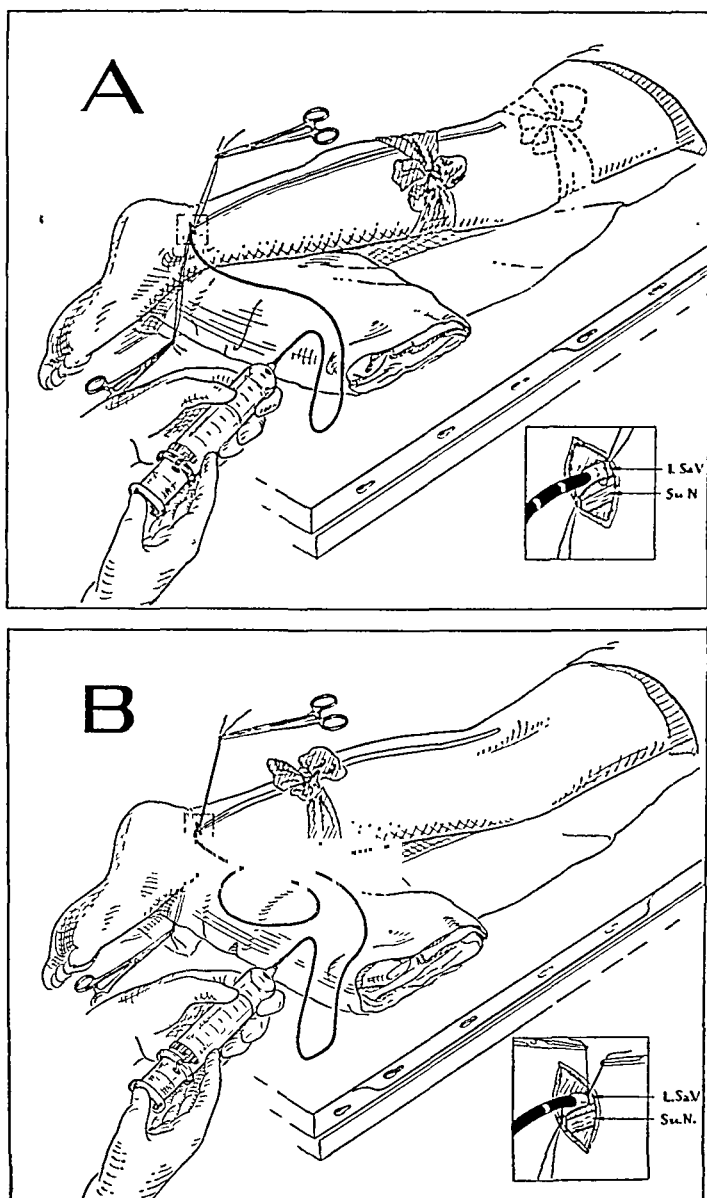


Fig. 2.—The technic of phlebography. *A*, catheter in the lesser saphenous vein, reaching as far as the saphenopopliteal junction. Radiography of the lower pelvis and upper three fourths of the thigh. (The use of the proximal tourniquet is not always necessary.) *B*, the tip of the catheter has been withdrawn to a point 4 to 5 cm. proximal to the site of phlebotomy. This phase of the procedure visualizes the upper three fourths of the leg and the lower one third of the thigh. (X-ray tube omitted from sketch.)

segments, the middle third of the line corresponds to the site of the incision. The lesser saphenous vein is in the posterior half of the incision (the half nearer the achilles tendon). The sural nerve runs deep and slightly lateral to the vein in very close proximity. Every precaution must be taken to avoid injuring or handling the sural nerve during the procedure. Between two holding ligatures of 000 plain surgical gut, only the distal one of which is tied at this time, a small incision is made into the wall of the vein and a no. 6 or 7 woven ureteral catheter<sup>8</sup> is introduced into the vessel. A length of the catheter is passed that has been formerly determined by measuring the distance between the proposed site of incision and the popliteal crease, the latter corresponding to the level of the point of junction of the lesser saphenous and popliteal veins (a very constant anatomic landmark). Introducing the catheter farther up (into the popliteal vein) requires fluoroscopic control and is not necessary. With the catheter in place, the blood pressure in the saphenous system is now determined.<sup>9</sup> Two tourniquets have been previously put in place untied, one 5 to 8 cm. above and one the same distance below the level of the popliteal crease; these tourniquets are now tied under sufficient tension to dimple the skin. The x-ray tube is so centered that a view is obtained of the lower part of the pelvis and the upper three fourths of the thigh on a 14 by 17 inch (35 by 43 cm.) film. Thirty cubic centimeters of 35 per cent iodopyracet (diodrast®) is now injected through the no. 18 gage needle connected to the catheter. The injection is done as fast as possible for the first 25 cc.; at the end of this portion of the injection an exposure (with the use of the Potter-Bucky diaphragm and of soft tissue technic) is made, the injection being continued slowly while the film cassette is changed for a second (stereoscopic) exposure. The second exposure is made at the moment the entire amount of dye has been injected. The first part of the injection takes from ten to fifteen seconds; changing the film and the second exposure require about the same length of time. The tourniquets are now removed, and the catheter is withdrawn far enough to leave only a length of 4 to 5 cm. in the lumen of the vein. The proximal ligature is tied taut with one knot around the catheter, and the leg is turned into full internal rotation. The position of the tube is changed to cover the lower third of the thigh and the upper three fourths of the leg. A tourniquet previously put in readiness around the lower leg 8 to 10 cm. above the site of incision is now tied and two stereoscopic exposures are made, the course of injection being the same as just described. The catheter is flushed in with 100 cc. of isotonic sodium chloride solution and withdrawn while the proximal ligature is kept taut and then tied square. The incision is washed out with saline solution and the skin is closed with a single vertical mattress stitch of silk. An elastic bandage is applied from toes to knee.

In every case bilateral phlebograms are taken. The second side is done twenty-four hours after the first one.

Certain precautions must be kept in mind concerning this procedure. Any damage to the sural nerve causes a very annoying and persistent neuralgic pain. Spilling the contrast medium will also result in this complication as well as in a tender induration around the phlebotomy (post-thrombotic limbs are very intolerant of this chemical insult). If

8. We have lately used a special catheter made for intracardiac catheterization. This has some advantages over the ureteral catheter.

9. Tyson, M. D., and Goodlett, W. C.: Venous Pressure in Disorders of the Venous System in the Lower Extremities, *Surgery* 18:669 (Dec.) 1945.

any resistance is encountered in passing the catheter, the catheter should be stopped at the point and injection be made at a lower level than usual; the results will usually still be satisfactory, whereas manipulation of the catheter may break the wall of the vein and permit extravasa-

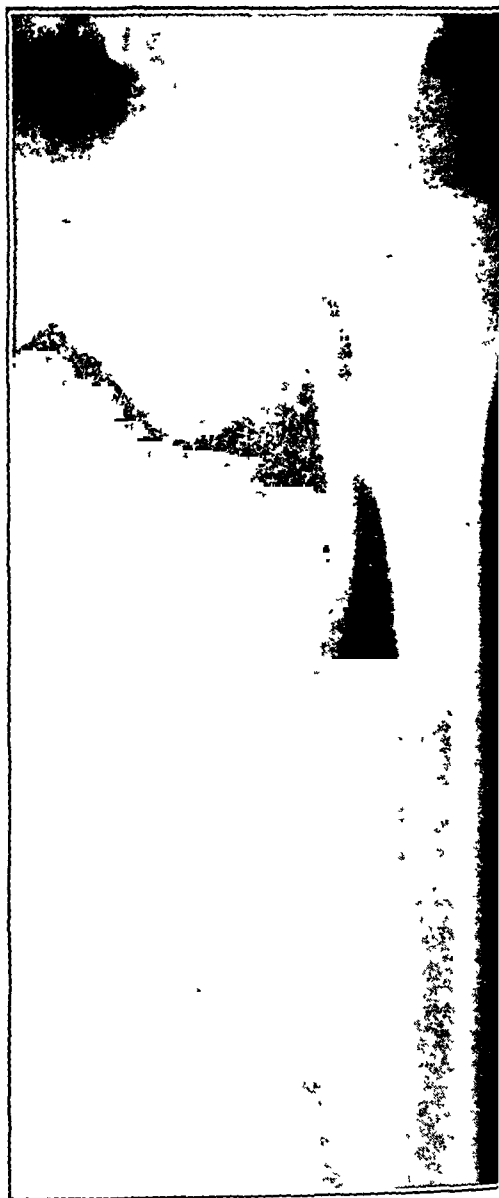
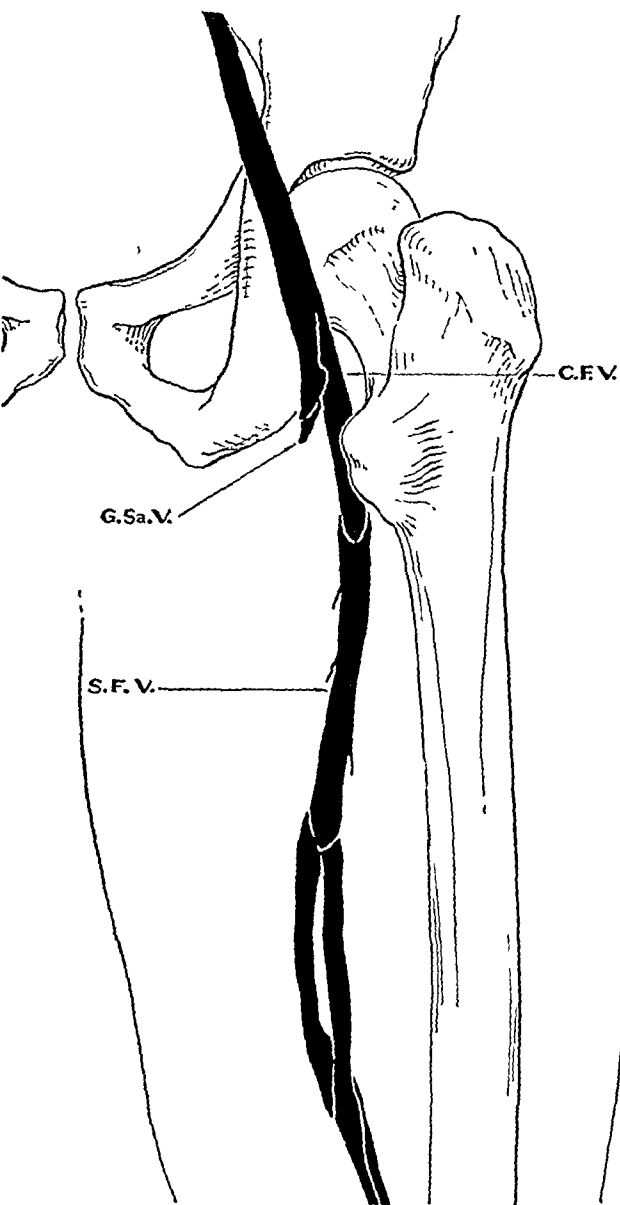


Fig. 3.—Normal phlebogram (posteroanterior) of the right femoral system. The lower superficial femoral vein is bifid. This figure should be compared with figure 5, which represents the opposite limb of this patient. *C.F.V.* indicates the common femoral vein, *G.Sa.V.*, the greater saphenous vein; *S.F.V.*, the superficial femoral vein.

tion of the medium. If one attempts to pass the catheter above the popliteal crease without fluoroscopic control, it may run through a large

communicating branch, which is fairly constant, into the greater saphenous vein and completely spoil the result. Phlebography done in this manner is not always an ambulatory procedure. Patients with no residuals in the leg can continue with their work, but most others should be hospitalized.

Iodopyracet is a safe preparation, but serious reactions may occasionally occur with its use. Each patient should have an intraoral and intravenous test dose at least an hour before administration. Although the amount used by us is large (60 cc. for each side), the excretion of the drug is rapid. In the early cases we followed the course of excretion by K.U.B. (kidney-ureter-bladder) plates and determina-

TABLE 18.—*Results of Phlebography*

	Number of Limbs	Number of Cases	Number of Phlebograms
Totals .....	..	31	46
Technics of phlebography .....			
Miscellaneous .....	..	8	19
Successful results.....	..	0	0
Catheterization of lesser saphenous vein.....	..	23	46
Successful results.....	37	..	40
Unsuccessful results.....	..	..	6
Findings on phlebograms .....			
Thigh .....	37	..	..
Thrombosis of superficial femoral vein above ligature .....	0	..	..
Thrombosis of superficial femoral vein below ligature .....	21*	..	..
Recanalization of superficial femoral vein below ligature .....	7	..	..
Recanalization of superficial femoral vein across ligature .....	0	..	..
Thrombosis of popliteal vein.....	12	..	..
Recanalization of popliteal vein.....	6	..	..
Thrombosis of deep femoral vein.....	0	..	..
Leg .....	37	..	..
Incomplete filling of deep veins.....	15	..	..
Filling with mottling.....	14	..	..

\* There was clinical involvement of the calf in 11 limbs and of the thigh in 5; clinical involvement was not present in 5.

tions of iodine in the urine. In patients with normal renal and hepatic function the renal pelvises are not visualized after four hours and the organic iodides disappear from the urine in twelve hours. As an added precaution, our patients had, besides routine physical and laboratory checks, screening tests of renal and hepatic function whenever there was a suspicion of impairment.

We saw no serious reaction in any of the cases. (A few patients were rejected because of positive sensitivity reactions.) In the earlier cases minor wound complications were fairly common (6 cases), but later these were entirely eliminated. Of 46 phlebograms, all but 6 gave adequate visualization for our purposes. The causes of failure were extravasation of the dye (1 case), extensive varicosities (1 case) and inadvertent catheterization of the greater saphenous vein (4 cases).

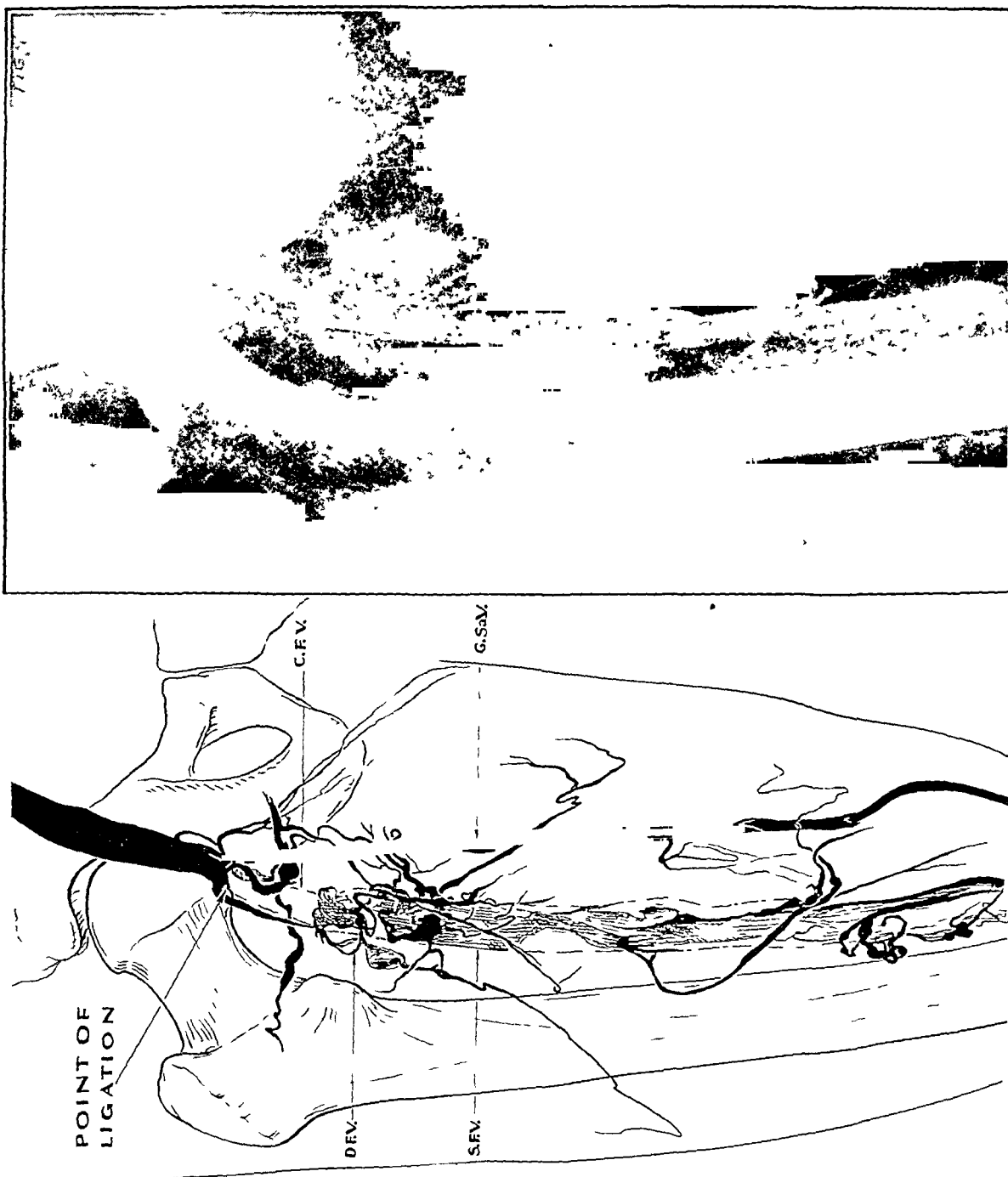


Fig. 4.—Phlebogram of the left femoral system twenty-four hours after ligation of the left common femoral vein for post-operative phlebothrombosis. There was strong clinical evidence of involvement of the calf but no clinical sign of thrombosis above the popliteal vein. The phlebogram shows massive thrombosis of the superficial femoral vein. Only the earliest, narrow and scanty radicals of the collaterals to develop later can be seen. The main drainage channel of the limb at this time is the greater saphenous vein. *D.F.V.* indicates the deep femoral vein, other abbreviations are as in the foregoing figures.



Fig. 5.—Phlebogram of the left femoral venous system thirty-six months after ligation of the left common femoral vein for phlebo-thrombosis (same patient as in figure 3). The superficial femoral vein has recanalized. *P.o.V.* indicates the popliteal vein.

(The technical difficulty created by large and numerous varices can sometimes be obviated by applying an elastic bandage.)

Only 2 patients were rejected for phlebography on account of the post-thrombotic changes in the legs.

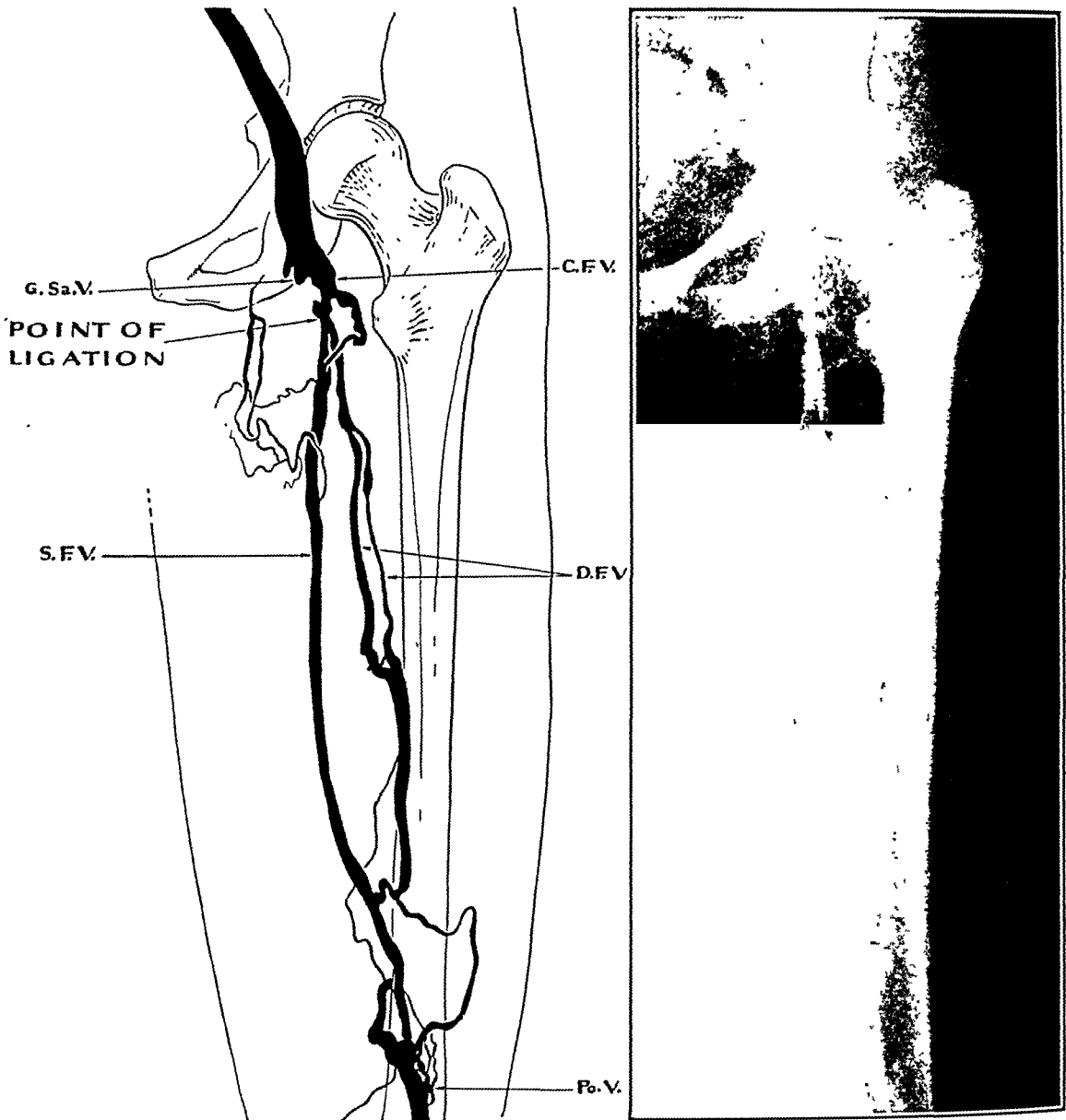


Fig. 6.—Phlebogram of the right femoral venous system twenty-two months after ligation of the superficial femoral vein for phlebothrombosis. The superficial femoral vein has remained patent and is probably functional by way of short collaterals around the point of ligation.

It must be stressed that this method is not proposed as a diagnostic procedure in acute phlebothrombosis. We do not believe that phle-

bography is necessary or helpful in establishing such a diagnosis. The method may, however, have usefulness as a differential diagnostic aid in cases of chronic swelling of the leg.

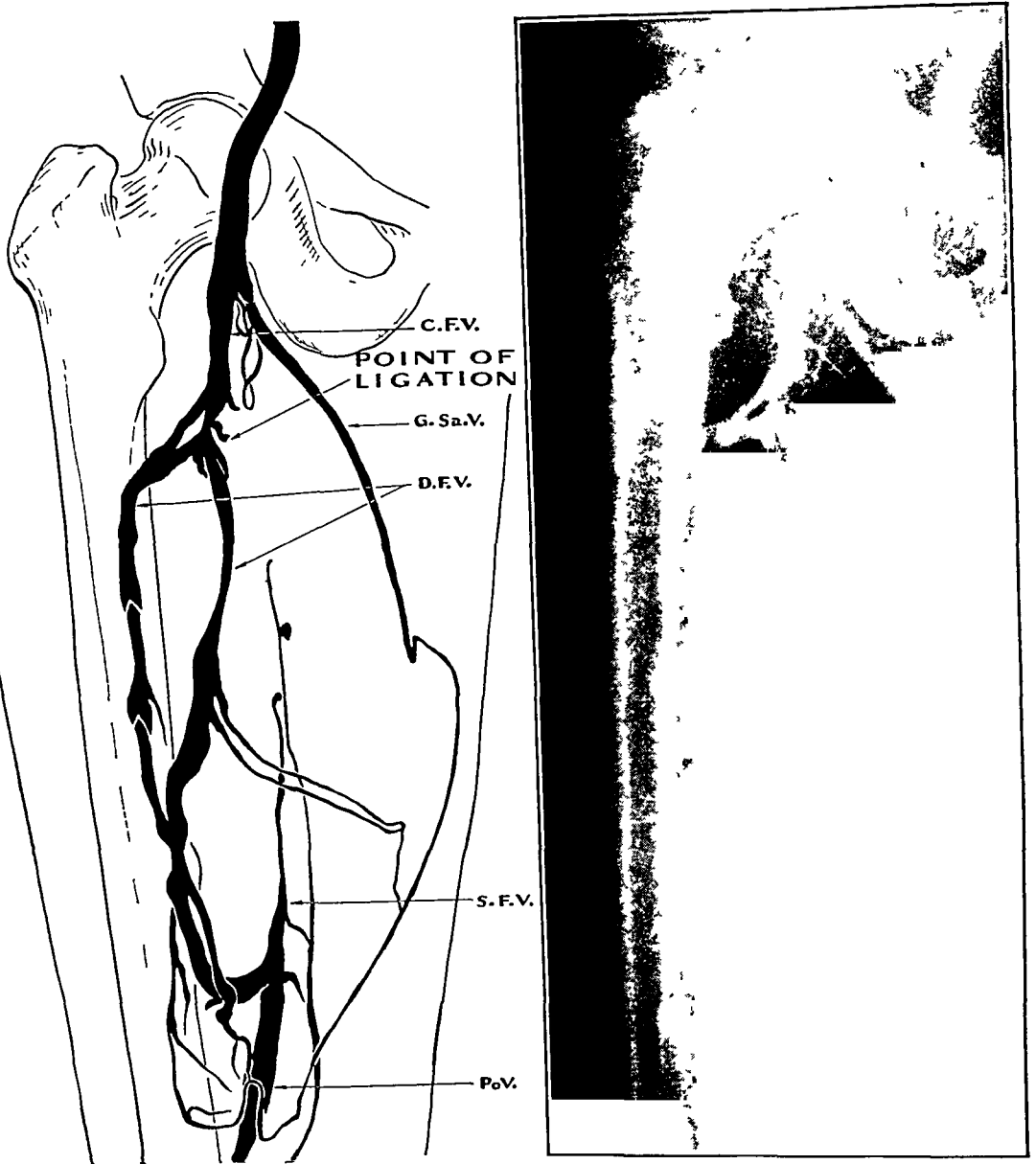


Fig. 7.—Phlebogram of the left femoral venous system forty-two months after ligation of the superficial femoral vein for phlebothrombosis. The superficial femoral vein has become thrombosed and shows partial but ineffectual recanalization. The deep femoral vein is the main drainage channel. The greater saphenous vein shows filling through a communicating branch.

As shown in table 18, we obtained phlebograms in 31 cases of vein ligation. In all but 2 cases the phlebograms were bilateral; in some



cases more than 1 phlebogram was taken on a side for special purposes or because of the failure of the first one. The 46 phlebograms on 37 limbs that form the subject of our further comments were all obtained with the catheterization technic.

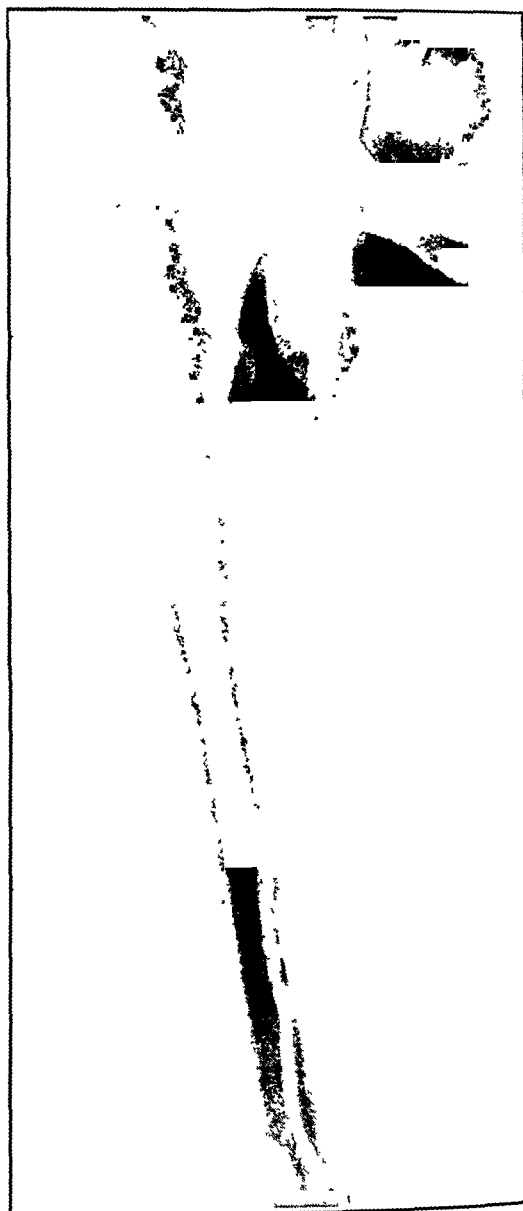
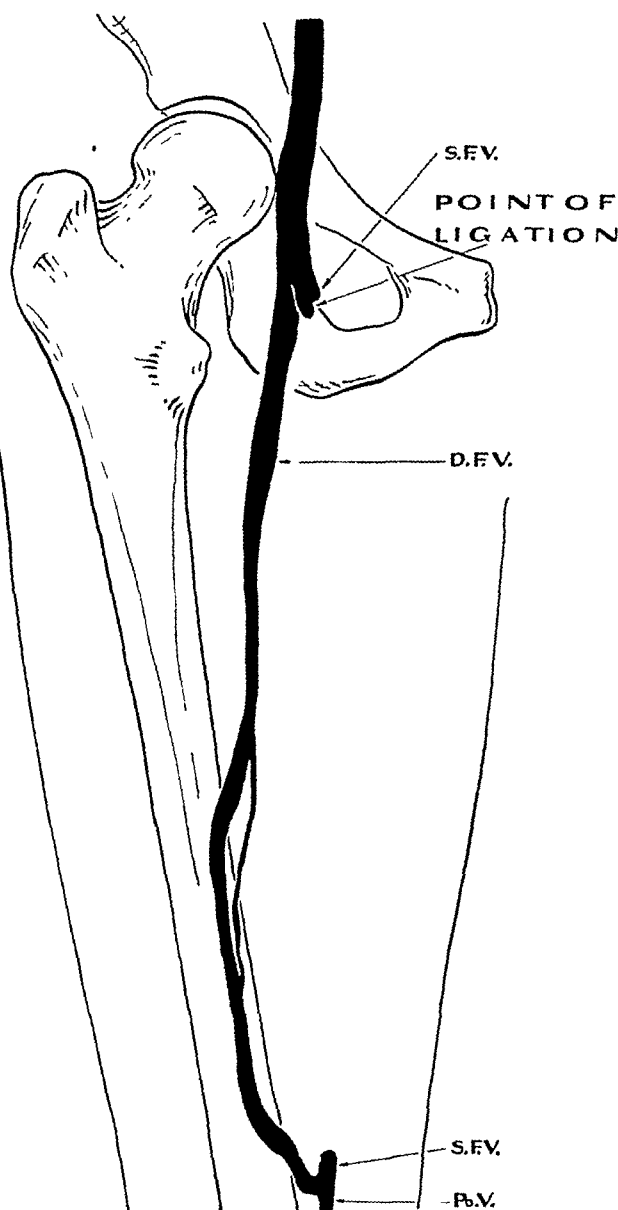


Fig. 8.—Phlebogram of the left femoral venous system eighteen months after ligation of the superficial femoral vein for phlebothrombosis. The superficial femoral vein has been almost completely obliterated by thrombosis. The deep femoral vein is the only draining pathway; its communication with the popliteal vein before ligation must have been direct and very ample.

*Phlebographic Observations.*—Any interpretation of phlebograms must be prefaced by a remark of caution. The evidence of thrombosis

in a phlebogram is negative—a failure of a vein or a segment of vein to fill with the contrast medium. Even if the technic is reliable and the clinical evidence supports the roentgenographic pattern, a given filling defect may be due to causes other than a clot in the lumen of

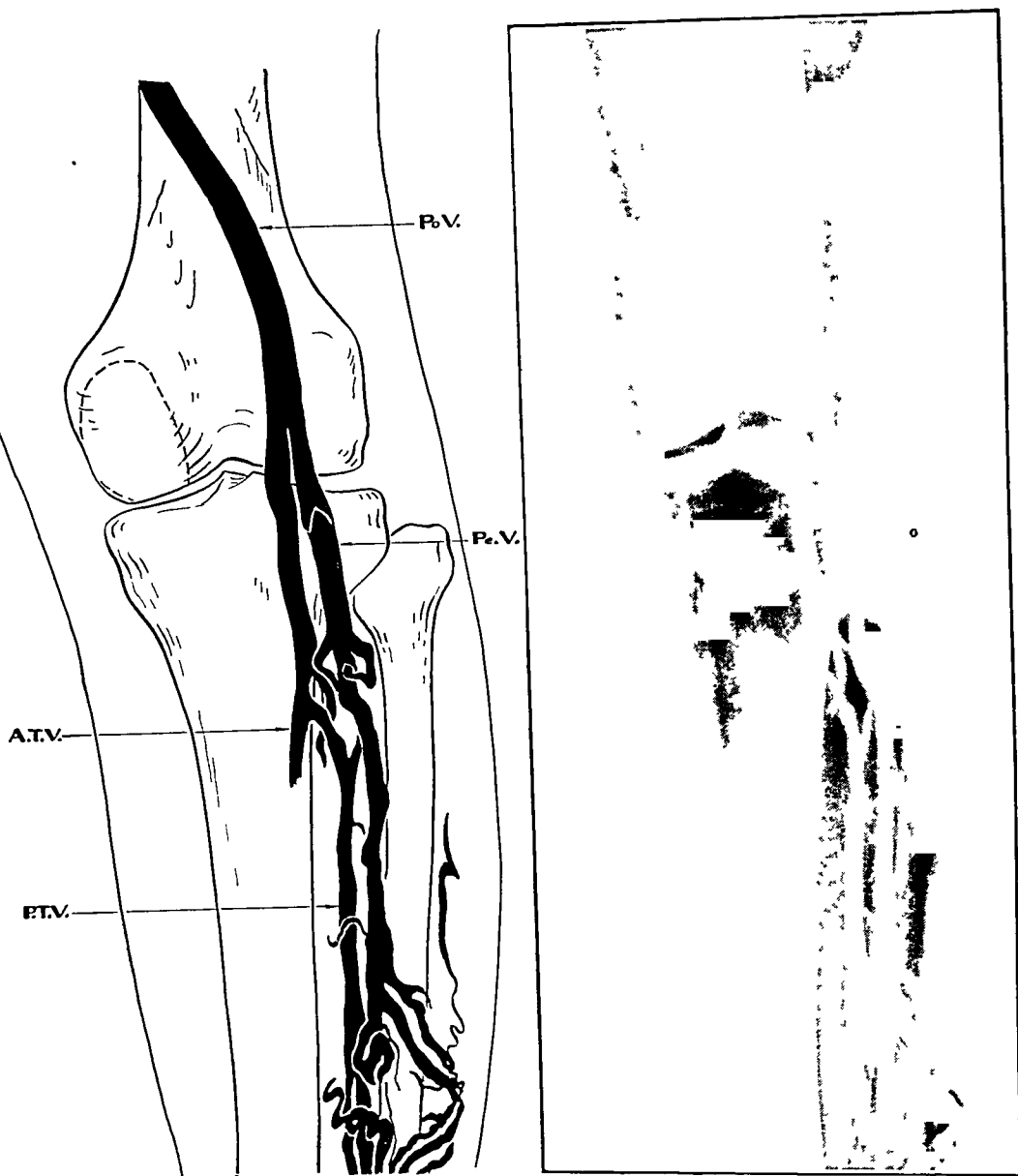


Fig 9—Normal phlebogram of the right leg and lower part of the thigh. The anterior tibial vein is not filled sufficiently to allow its visualization through the superimposed tibia. The superficial communications of the peroneal vein are unusually rich and large.

the vein. The dye follows the path of least resistance, and anatomic variations will occasionally lead it away from channels that may be

functionally open. In many situations, therefore, interpretation of a pattern may be a matter of opinion.

The aim of our inquiry in the phlebographic investigation was, as stated before, to follow, as far as possible, the changes in the process of thrombosis in the involved vein from the time of ligation for an indeterminate length of time. The ideal way to achieve this aim would be to obtain serial phlebograms on a number of patients in chronologic order and to correlate the findings case by case. Such a study is now under way, but its practical obstacles are serious. At present we have data only on the different ages of the evolution of thrombosis in different persons (the interval between the time of ligation and the time of phlebography ranging from one day to fifty-seven months).

In attempting to reconstruct the process of thrombosis from the phlebographic evidence of its phases at various time intervals and in different subjects, we selected the following features to be looked for and be compared: presence or absence of thrombosis in the common femoral or superficial femoral veins (according to the level of ligation) below and above the ligature; presence of thrombosis in the deep femoral and popliteal veins; occurrence of recanalization in any one of these veins; presence of thrombosis and recanalization in the veins of the leg; role of the greater saphenous vein in the drainage of the leg when the deep veins are involved; presence and adequacy of collaterals (in the surgical and not in the anatomic sense), including the presence of valves, in both the thigh and the leg. The important observations with respect to these questions are also summarized in table 18.

In the thigh there were two observations of interest that recurred with great constancy: There was no instance of thrombosis in the deep femoral vein after ligation of the superficial femoral vein, and the ligated superficial femoral and common femoral veins never showed evidence of thrombus formation above the site of ligature. The fact that the deep femoral vein remained always patent after ligation of the superficial femoral vein is of great importance from the fact that the vessel (as will be seen) is the most useful collateral pathway after ligation in a large proportion of cases. The complete absence of extension above the ligature in the surgically interrupted venous trunks is significant since many surgeons have feared that such an extension may be a common event; the fact that a spread of the clot above the ligation does not take place is a strong confirmation of the soundness of the procedure of ligation.

The thrombosis of the superficial femoral vein after ligation of that vein in a considerable proportion of the cases that had had no clinical evidence of involvement of the thigh (or any involvement at all) was a surprising observation. This fact would tend to support the assumption that ligation in itself may precipitate clotting in the superficial

femoral trunk. The anatomic circumstance that the superficial femoral vein often receives few tributaries from the level of its junction with the deep femoral vein to the lower third of the thigh seems to predispose

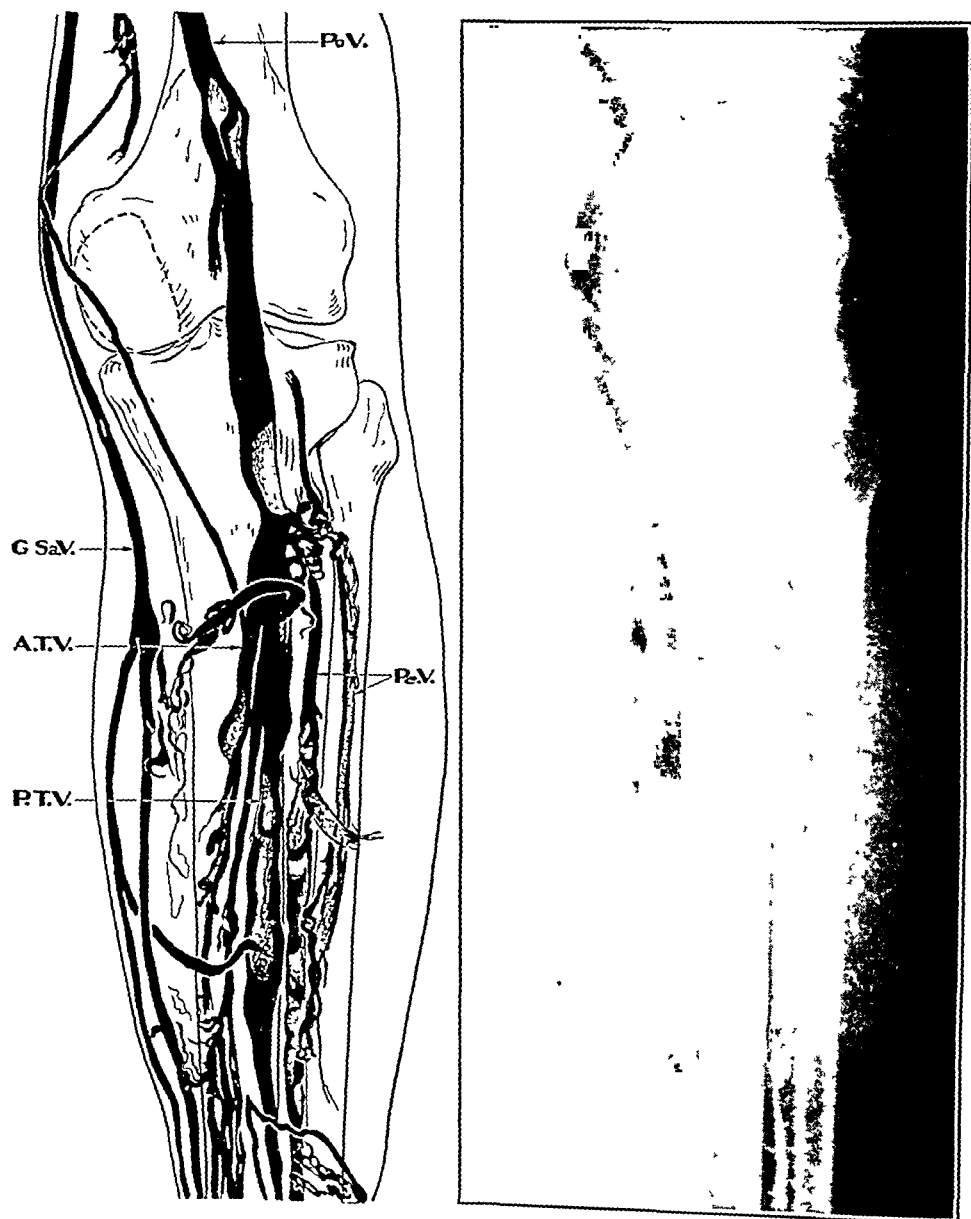


Fig. 10—Phlebogram of the right leg and lower part of the thigh eighteen hours after ligation of the superficial femoral vein for phlebothrombosis (same case as figure 4.). There is moderately advanced thrombosis of all the deep veins of the leg and of the popliteal vein.

this vein to thrombosis after ligation, since when this vessel is interrupted below the level of the deep femoral vein its trunk is turned into a

practically stagnant channel as far down as the lower end of Hunter's canal. Interestingly, in 7 instances it was exactly this segment that had been closed off by thrombosis. Recanalization when it takes place is rudimentary and probably nonfunctional (valveless) according to phlebo-

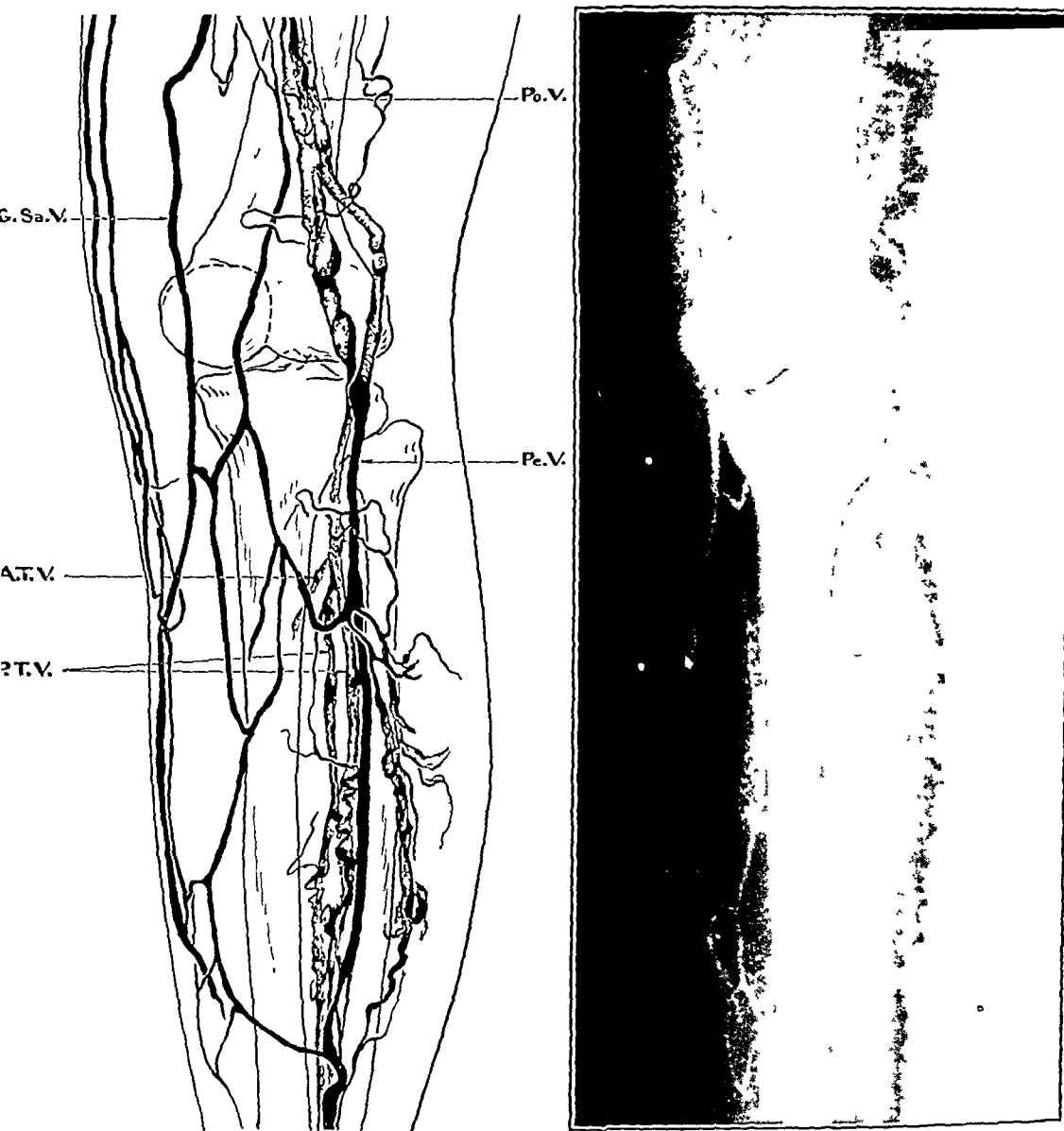


Fig. 11—Phlebogram of the right leg and lower part of the thigh forty-eight hours after ligation of the superficial femoral vein for phlebothrombosis. The thrombosis is much more advanced than in figure 10. Part of the peroneal vein is curiously spared. Note here, as in figure 10, the heavy filling of the greater saphenous system, on which the main burden of drainage falls.

graphic evidence. There was no example of recanalization of the venous trunk across the point of ligation.

The importance of the deep femoral vein in the formation of collateral circulation is shown by the fact that in every instance of thrombosis of the superficial femoral vein it appears to have taken over the



Fig 12—Phlebogram of the left leg and lower part of the thigh thirty-nine months after ligation of the superficial femoral vein for phlebothrombosis. The normal pattern of the deep veins of the leg is replaced by an irregular configuration of venous channels, some of which show mottling. The popliteal vein does not fill. The venous return of the leg is, from all appearances, almost entirely through the greater saphenous vein.

entire load of venous drainage of the thigh. It practically replaces the superficial femoral vein.

In the thigh the phlebographically demonstrable collateral circulation after ligation is determined by the level of ligation and the extent of the thrombotic process. Three definite patterns were noted. 1. In the only case of ligation of the common femoral vein adequately investigated (another such has so far been studied only twenty-four hours postoperatively [fig. 4]) three collateral circuits had developed (fig. 5). An inferior circuit was formed for communication between the deep femoral and superficial femoral veins (which partially recanalized); a medial superior circuit appeared to connect the superficial femoral with the common femoral and thence with the obturator and internal pudendal veins; a lateral superior circuit was evident between the deep femoral and inferior gluteal veins. 2. The second collateral pattern is a simple one; it is established when the superficial femoral vein is ligated but remains open. In such cases the important new pathways are those joining together deep and superficial femoral venous trunks in the lower part of the thigh (fig. 6). The third pattern comes about when the superficial femoral vein is thrombosed after it has been ligated. Regardless of the state of recanalization of the superficial femoral vein, the main collateral branches in this instance develop between the deep femoral and the popliteal vein (figs. 7 and 8). As in the former pattern, collaterals of lesser importance may appear also between the common femoral and superficial femoral veins around the site of ligation.

The interpretation of the changes in phlebograms of the leg is less reliable (figs. 9, 10, 11 and 12). The factors that may cause ambiguity, mentioned in an earlier paragraph, hold particularly true here. The rich superficial network of veins may both obscure the configuration and interfere with the filling of deep veins (which are often difficult to see owing to the osseous structures). It can be stated with fair certainty, however, that recanalization in these veins is very common and complete. Only 3 definite instances of marked defects of filling were noted in 26 limbs that had been operated on three months or more before. Evidences of irregular filling were present in 14 cases. Since valves in the deep veins of the legs are hard to demonstrate even in normal phlebograms, it is difficult to make inferences as to the functional state of a phlebographically recanalized leg vein. The collateral channels in the leg are for the most part superficial; at times the greater saphenous appears to carry almost the entire burden of providing a drainage channel around the knee (fig. 12). The significance of this fact is great in relation to the potential dangers of tying or stripping the greater saphenous vein in cases of old thrombophlebitis.

#### SUMMARY

The early and late changes that occur in the limbs after surgical vein interruption were investigated by clinical and roentgenographic means in 100 cases with 146 vein operations affecting 150 extremities.

Some of the clinical characteristics of the cases composing the series are summarized. The advanced state of thrombotic disease at the time of ligation in a high proportion of these cases is pointed out. In a clinical follow-up survey the success of vein ligation in the prevention of the embolic complication of thrombosis is evaluated and the effect of the operation on the evolution of the local thrombotic process is analyzed. After a short description of a phlebographic technic by catheterization of the lesser saphenous vein, the roentgenographic findings of 46 phlebograms obtained in 23 cases and involving 37 limbs are presented.

#### CONCLUSIONS

1. In a relatively small group of cases (100 cases with 146 operations) the therapeutic ligation of one or the other of the main venous trunks draining the lower limbs, carried out under proper indications and in the right manner, has been found highly effective in the prevention of pulmonary embolism. Only 1 nonlethal embolic incident occurred after ligation that could be attributed to the failure of the method.

2. A large proportion (80 per cent) of the patients show the appearance of a new swelling or an aggravation of the existing swelling immediately after ligation. After the first postoperative month (and often earlier) this swelling shows consistent improvement for a year if a few simple precautions in the care of the limb are observed. Eventually the condition of a third of the limb returns to normal, and in the remainder, with very few exceptions (less than 2 per cent of the total), the persistent residual changes are not severe enough to interfere with the pursuit of a normal, gainful life.

3. When the superficial femoral vein is ligated directly distal to its junction with the deep femoral vein, there is strongly suggestive evidence in the phlebograms of the ligated limbs that ligation per se precipitates clotting in the segment of the superficial femoral vein lying directly distal to the ligature. There is no proof, however, that this extension of thrombosis adds in any important degree to the permanent sequelae of the pathologic process.

4. With the same technic of ligation (as mentioned in the preceding paragraph) thrombosis has not been noted in the phlebograms proximal to the ligature or in the deep femoral vein. The freedom from clotting of the deep femoral vein permits the formation of an excellent collateral pathway in practically every case of ligation of the superficial femoral vein.

5. As shown by phlebograms collateral circuits of drainage in the thigh are formed in definite patterns that correspond to anatomic expectations and depend on the level of ligation and the extent of thrombosis;



they appear ample. There was no instance of reopening of the venous lumen across the site of ligature. Recanalization of the thrombosed superficial femoral vein has not been seen to have a useful role in the hemodynamic readjustment after ligation.

6. Phlebograms disclose that the deep veins of the leg undergo recanalization in a great proportion of cases. However, restitution of effective venous drainage is in such cases, too, often dependent on the collateral channels which in the majority of instances appear to be superficial (mainly the greater saphenous vein and its tributaries).

Dr. Howard P. Doub and the members of his staff, particularly Mr. Carl Anderson, cooperated in obtaining the phlebograms described in this study.

# INTRAVASCULAR AGGLUTINATION (SLUDGED BLOOD), VASCULAR STASIS AND SEDIMENTATION RATE OF THE BLOOD IN TRAUMA

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AND

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IT IS WELL known that drawn blood does not possess the same properties as circulating blood. With the knowledge that blood usually undergoes certain changes as soon as it comes into contact with any material that is not normally a part of the vascular tree, it would appear natural to make observations concerning its physiologic reactions while it is passing unmolested through the vascular bed. To achieve this end not only must one maintain the physiologic state of the tissues in question but microscopic examination requires illumination and the source of light must not be a source of heat or the observations become invalid.

Since the discovery of circulation in 1629 by William Harvey, it is interesting to note how little attention has been paid to the microscopic study of circulation in the living tissues. Special technics and careful manipulation of tissues are required. Methods used in this study are similar to those used by Melvin Knisely<sup>1</sup> and his workers, who have pioneered this field in America. As will be observed in the historical survey to follow, the phenomenon of red cell agglutination has been studied principally in relationship to disease and infection. Only recently has Knisely associated this phenomenon with trauma, and he has coined the term "sludge" to describe the vascular changes which he observed.

The following presentation is a study of both the area of local trauma and the vascular bed remote from the traumatized area. Heat, cold, tourniquet and crush injuries were used. The phenomenon of intravascular agglutination of erythrocytes has been observed in association

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Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 18, 1949.

<sup>1</sup> Knisely, M. H.: An Improved Quartz Rod for Living Tissue Illumination, *Anat Rec* **71**:503-508 (Aug.) 1938.

with these forms of trauma, and an attempt has been made to correlate that which is transpiring as a vital changing process with knowledge of suspension stability of the blood and the present concepts of pathology. The fate of these agglutinated clumps of red cells and the possible role of the liver in this regard have been studied.

It was soon evident in this work that descriptions, still photographs, microscopic sections and diagrams were inadequate to record and demonstrate the progressive changes that occur in the vascular bed. Accordingly, colored motion pictures were taken. Altered dimensions of structures and changes in rate of vascular processes were thus preserved as a permanent record.

#### HISTORICAL SURVEY

From time immemorial, the most favored remedy for nearly all illnesses was blood letting. Usually the evacuated blood differed from healthy blood in that the blood "cake" settled out more quickly, leaving a buffy coat behind. The suspension stability of the blood had been altered in the diseased state. Thus Hippocrates' humoral theory of disease was evolved.

After the discovery of capillaries and erythrocytes by Malpighi, attention was turned to the microscopic changes in the vascular bed. In Boerhaave's "Aphorisms"<sup>2</sup> (1709) it is stated in the description of inflammation that the pathologic process which is the root of many evils consists in stagnation of the blood in the capillaries, whether due to narrowing of the latter through outward influences, mechanical or chemical, or because the blood has become more thickly flowing.

John Hunter<sup>3</sup> in 1786 described pathologic blood thus:

In all inflammatory dispositions in the solids whether universal or local, the blood has an increased disposition to separate into its component parts, the red globules becoming less uniformly diffuse and their attraction to one another becomes stronger, so that blood when out of the vessels soon becomes cloudy or muddy and dusky in its color, and when spreading over any surface it appears mottled, the red blood attracting itself and forming spots of red.

Cohnheim's<sup>4</sup> lectures on general pathology (1877) drew attention to the changes in erythrocytes in his study of inflammation. The presence of vessels packed with immobile masses of red cells was referred to as "stasis," which he believed due to blood coagulation. Most workers since have believed that this phenomenon was simply due to leakage of plasma, thus leaving the erythrocytes stranded in

2. Boerhaave: *Aphorismi de cognoscendis et curandis morbis*; 1709; German Translation, Berlin, 1763, p. 146.

3. Hunter, J.: *Works of John Hunter, F.R.S.* edited by J. S. Palmer: Longmans, Rees, Orme Green & Longmans, London, 1835, vol. 1, p. 235.

4. Cohnheim, J.: *The Circulation*, in Cohnheim's *Lectures on General Pathology*, London, New Sydenham Society, 1889, vol. 1.

the lumen of the vessel. Von Recklinghausen, quoted by Tannenberg,<sup>5</sup> differentiated stasis from simple cessation of flow, in that in the latter the red cells remain quite discrete, being suspended in the plasma.

Workers who followed inferred that reconstitution of flow in an area of stasis would always be in the form of discrete cells. Thus the theory of agglutination of red cells in stasis was relegated to the background.

Hüter,<sup>6</sup> in 1786, described the microscopic picture of the nictitating membrane in health and disease. Following the experimental production of septicemias and wound infections in dogs, he found circulating clumps of red cells in the capillaries of the nictitating membrane. These clumps often produced capillary stasis intermittently and then were swept once again into the circulation.

Studies of eclampsia by Schmorl,<sup>7</sup> in 1893, showed hepatic thrombi to be present in the finest branches of the portal system. In 1902 Flexner<sup>8</sup> reported intravascular agglutination of red cells in the region of many infected tissues, as shown by pathologic sections.

Normal circulation was again described by Arey<sup>9</sup> in 1918. He emphasized the fact that red cells remained quite discrete in normal vascular flow, exhibiting no tendency to stick together or even to show rouleau formation.

Correlation of sedimentation rate of the blood with the nature of the flow in the retinal vessels, was attempted by Ploman<sup>10</sup> in 1920. He found that with the compression of the central artery in perfect health the microscopic picture was one of smooth flow. In contrast, people with elevated sedimentation rate showed flowing clumps of erythrocytes.

The great works of Robin Fåhræus,<sup>11</sup> the first of which appeared in 1921, attracted the attention of the whole world to erythrocyte

5. Tannenberg, J., and Fischer-Wasels, B.: *Handbuch der normalen und pathologischen Physiologie*, 1927, vol. 7, p. 1496.

6. Huter, C.: *Die febrilen Störungen des Blutkreislaufs, mikroskopisch beobachtet an der Palpebra tertia septisch und pyämisch inficirter Warmblüter*, *Centralbl. f. med. Wissenschaft.* **14**:505-510, 1876; *Die cheilo-angioskopie, eine neue Untersuchungs-methode zur physiologischen und pathologischen Zwecken*, *ibid.* **17**:225-27 and 241-45, 1879.

7. Schmorl *Untersuchungen über Puerperal-Eklampsie*, Leipzig, 1893, p. 15.

8. Flexner, S.: *On Thrombi Composed of Agglutinated Red Blood Corpuscles*, *J. M. Research* **8**:316-321, 1902.

9. Arey, L. B.: *Observations on the Shape of the Erythroplastid in the Wing of the Bat*, *Anat. Rec.* **14**:135-139, 1918.

10. Ploman, M. O.: *Demonstration ophthalmoscopique des variation de stabilité dans la suspension des globule rouges*, *Ann. d'ocul* **52**:569-580, 1920.

11. Fåhræus, R.: (a) *The Suspension Stability of the Blood*, *Acta med. Scandinav* **55**:1-228, 1921; (b) *The Suspension Stability of the Blood*, *Physiol. Rev.* **9**:241-274 (April) 1929.

agglutination. The suspension stability of the blood was thus established as a physiologic phenomenon. Increase in the sedimentation rate of erythrocytes was found to be due to an increased tendency of the cells to form aggregates. He demonstrated a high correlation between the sedimentation rate of erythrocytes and the clumping tendency of circulating erythrocytes in the human nail bed. Experimental injections of hydrophylic colloids, such as gelatin, produced a simultaneous elevation of the sedimentation rate and intravascular agglutination of circulating red cells, as seen in the mesentery of the guinea pig.

The European school recognized the importance of stasis in the inflammatory reaction especially as shown by Ricker<sup>12</sup> and Kreyberg,<sup>13</sup> but it was Tannenberg<sup>5</sup> who, in 1927, contributed an important addition to the theory of vascular stasis. He felt that there was something more than a passive accumulation of red cells. There seemed to be a decreased suspension stability of the blood, with resulting agglutination of red cells into a red homogeneous column, in which individual red cells were not detectable (microscopically *in vivo*).

Many investigators have since demonstrated the relationship between agglutinated circulating erythrocytes and disease, including Freedlander and Lenhart<sup>14</sup> in 1922, Ruedemann<sup>15</sup> in 1933 and Müller<sup>16</sup> in 1937. Youngner and Nungester,<sup>17</sup> in 1944, showed that type III pneumococcus polysaccharide produced generalized intravascular agglutination *in vivo*.

The term "sludged blood" was used by Knisely and his co-workers as a comprehensive term to describe abnormal blood flow associated with pathologic states. The name was suggested by the slow uneven flow which may be seen in the general circulation or in areas of tissues exposed to local trauma. Sludge also refers to the agglutinated clumps themselves, and in his article he described several types of sludge according to the size and friability of the masses. The complete blockage of vessels, which has been called vascular stasis in the past, is described as thrombosis by Knisely.

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12. Ricker, G.: *Pathologie als Naturwissenschaft*, Berlin, Julius Springer, 1924.

13. Kreyberg, L., and Rotnes, L.: *Acta path. et microbiol. Scandinav.* **11**:162, 1932.

14. Freedlander, S. O., and Lenhart, C. H.: *Clinical Observation on the Capillary Circulation*, *Arch. Int. Med.* **29**:12-32 (Jan.) 1922.

15. Ruedemann, A. D.: *Conjunctival Vessels*, *J. A. M. A.* **101**:1477-1481 (Nov. 4) 1933.

16. Müller, O.: *Die feinsten Blutgefäße des Menschen in gesund und kranken Tagen*, Stuttgart, 1937-1938.

17. Youngner, J. S., and Nungester, W. J.: *The Effect of Type III Pneumococcus, Polysaccharide and Gelatin on the Circulation and Sedimentation Rate of Erythrocytes in Mice*, *J. Infect. Dis.* **74**:247-253 (May-June) 1944.

Knisely and his associates<sup>18</sup> first reported in 1941 intravascular agglutination in the living malaria-infected monkey, and they developed the concept of intravascular agglutination and its relationship to disease and trauma<sup>19</sup> and suggested that the circulating clumps might be a cause of general fluid loss in the body in such conditions as traumatic shock.<sup>20</sup> They also suggested the existence of abnormal phagocytosis of the red cells by the reticuloendothelial system in pathologic states.<sup>21</sup>

#### METHODS

Two principal methods have been used, one by transillumination and the other by reflected lighting of tissues. In the former, light is conveyed from a 500 watt bulb along a fused quartz rod. The tip of the rod is angulated upward to conduct the beam of light through the overlying tissues. This allows examination of tissues in relatively inaccessible sites. Heat is removed by a water cell filter interposed between the light and the rod. The terminal 6 inches (15 cm.) of the rod is tubular and conveys Ringer's solution, which emerges at the tip and bathes the under surface of the structure being examined. This absorbs most of the remaining heat in the rod.

Mammalian Ringer solution with 1 per cent ash-free gelatin, as suggested by Chambers and Zweifach,<sup>22</sup> was heated in a thermostatically controlled water bath, and, besides passing through the quartz rod tip, it was directed to allow a continuous flow over the upper surface of the structure, thus maintaining an isotonic and isothermic environment at all times. This continuous flow readily absorbed the small amount of heat which is inevitably produced when light strikes tissue, and it rigidly maintained body temperature plus or minus 1 degree C.

Several adjustable holders have been constructed to support the structures and to minimize movement from respiration and arteriolar pulsation. These factors have loomed most important in cinephotomicrography.

The second method of examination entails oblique illumination from a source of light attached to the microscope. This small focusing lamp was

18. Knisely, M. H.; Stratman-Thomas, W. K., and Eliot, T. S.: Observations on Circulating Blood in the Small Vessels of the Internal Organs in Living *Macacus Rhesus* Infected with Malarial Parasites, *Anat. Rec.* **79**:90, 1941.

19. Knisely, M. H., and Bloch, E. H.: Microscopic Observations of Intravascular Agglutination of Red Cells and Consequent Sludging of the Blood in Human Diseases, *Anat. Rec.* **82**:426 (March) 1942. Knisely, M. H.; Bloch, E. H.; Eliot, T. S., and Warner, L.: Sludged Blood, *Science* **106**:431 (Nov. 7) 1947. Brooks, H. F.; Dragstedt, L. R.; Warner, L., and Knisely, M. H.: The Sequence of Circulating Changes Following Severe Thermal Burns, *Anat. Rec.* **100**:644 (April) 1948.

20. Knisely, M. H.; Eliot, T. S., and Bloch, E. H.: Sludged Blood in Traumatic Shock: I. Microscopic Observations of the Precipitation and Agglutination of Blood Flowing Through the Vessels in Crushed Tissues, *Arch. Surg.* **51**:220-236 (Nov.-Dec.) 1945.

21. Knisely, M. H.; Bloch, E. H., and Warner, L.: Selective Phagocytosis: I. Det Kongelige Danske Videnskabernes Selskab, Copenhagen, *Biologisk Skrifter*, 1948, vol. 4, no. 7.

22. Chambers, R., and Zweifach, B. W.: Topography and Function of the Mesenteric Capillary Circulation, *Am. J. Anat.* **75**:173 (Sept.) 1944.

fitted with a heat-absorbing filter and connected to a transformer and rheostat. With experience the light could be adjusted to produce sufficient illumination, without undue heat or discomfort to a conscious patient. This method was used in the study of human subjects and larger animals.

Both binocular and monocular microscopes were used, with dry and water immersion lenses, allowing a magnification range of 7 to 400 diameters. With oblique illumination the binocular wide field microscope was attached to a swing arm mounting. Caliber of the vessel was determined by a micrometer scale mounted into the ocular. Cinema recordings were made by a Kodak

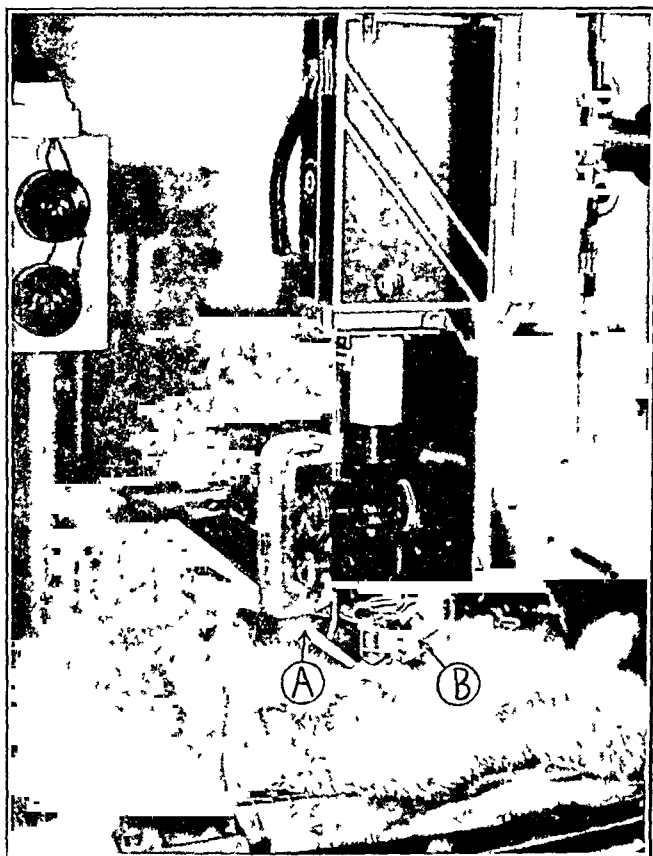


Fig. 1.—Quartz rod transillumination technic. *A*, quartz rod conducting light to tissue; *B*, insulated tube carrying Ringer's solution.

Special® camera mounted conveniently over the microscope. A still camera was similarly mounted.

Warm-blooded animals and human subjects were chosen for the study. Although cold-blooded animals, such as the frog, with erythrocytes 20 microns in diameter, are easier subjects to observe, the difference in constituent elements of the blood made them less desirable. The following animals were examined: 60 human subjects, 88 rabbits, 50 dogs, 10 guinea pigs, 7 mice and 12 rats.

The omentum, bowel mesentery, liver, nictitating membrane, scleral conjunctiva and iris vessels were the areas used for study. It was thus possible to

correlate findings in the different parts of the vascular tree of the same animal. To observe the omentum or mesentery, the animal was carefully opened through the linea alba, sharp scissors being used to minimize hemorrhage and trauma and thus preserve the normal circulation. Organs were lightly handled by fingers or dull hooks moistened with Ringer's solution and placed on a plastic ring under which the quartz rod could be adjusted while they remained constantly bathed in isothermic Ringer's solution. The nictitating membrane was examined by carefully insinuating the dull tip of the quartz rod between the sclera and membrane. The retinal vessels were studied in the rat only, in which the whole eyeball was



Fig. 2—Close-up view of transillumination technic A, plastic holder with omentum in place; B, tubes conducting saline solution

transilluminated by the quartz rod. The scleral conjunctiva was studied by reflected light, with manual retraction of the lids. Conjunctivitis or other infections of the eye had to be ruled out.

Knisely's observation that barbiturates did not induce any recognizable agglutination of the cells in many hundreds of animals was confirmed, and this type of anesthesia was used throughout. The human sclera could be examined in the fully conscious patient quite satisfactorily. At all times minimal amounts of anesthetic were used to insure adequate respiration and adequate cardiac function.



*Local Trauma.*—Animals were examined for the presence of clumping or stasis before each experiment (usually in an eye), and only sludge-free animals were used. Local trauma was studied as applied to the omentum and mesentery. Cold was applied in the form of 20 cc. of Ringer's solution at 3 C., ejected from a syringe, as well as solid carbon dioxide in direct contact with the tissues for one to two minutes. To study the effect of heat, Ringer's solution at various temperatures up to 80 C. was applied. Direct trauma involved injury to the mesentery, bowel or omentum by manual manipulation for periods up to ten seconds with fingers moistened with saline solution or a more localized type of injury from pressure by a blunt probe. As far as possible the same microscopic field was visualized and photographed before and after trauma.

*General Systemic Effect.*—In this phase of the work the lower extremities of sludge-free healthy anesthetized animals were clipped, exposed to burns, crushing injury or prolonged arterial tourniquet and the effect observed in the vascular tree remote from the area traumatized. Standard 6 per cent burns from boiling water were produced in the extremities after the method of Drinker. Fifteen per cent flame burns were used to produce uniform erythema. Crushing injuries were produced under light pentobarbital sodium (nembutal®) anesthesia by 500 rapid light blows with a rubber mallet, avoiding fractures and internal hemorrhage. Arterial tourniquets were applied high up on the thigh for three to fifteen hours. The degree of trauma has been designated as mild when represented by immersion in boiling water for one and three seconds, and hammer injuries. Severe trauma included exposure to boiling water for five to thirty seconds (rabbits and dogs).

#### OBSERVATIONS

1. *Normal Circulation.*—The technic of observing tissue by trans-illuminated light was developed to the point that the abdominal viscera could be observed continuously in a lightly anesthetized animal for periods up to four hours, during which time normal circulation appeared to be maintained. The addition of 1 per cent gelatin to mammalian Ringer solution<sup>22</sup> was found necessary to prevent petechial hemorrhages and evidence of edema after prolonged observation.

The vascular bed differed in minor respects in the various areas examined. Arterioles and venules could be recognized by their size, rate and direction of flow, thickness of wall, pulsations and whether the branches were subdividing or rejoining the main vessel. In the omentum and mesentery, the arteriole terminus, or metarteriole, continued as a thoroughfare channel (Chambers and Zweifach<sup>22</sup>) which, in turn, drained directly into a venule. Here the flow was rapid, and numerous capillaries left each channel to anastomose and reenter at its venular end. There was variation in the length of capillaries, and their diameters ranged from 6 to 15 microns. No evidence of capillary contractility in the mammal has been observed. With experience, a rhythmic variation in diameter, suggesting alternate vasoconstriction and dilation, could be observed in the metarterioles. This has been called "vasomotion" by Chambers and Zweifach. Arteriovenous shunts

were commonly seen as short muscular vessels connecting arteriole and venule.

The flow under normal conditions in all vessels was rapid and smooth. Normal rate in arterioles and venules was indicated by the inability to see individual red cells. In these vessels longitudinal streaks were observed and interpreted as evidence of laminar flow,<sup>23</sup> which denotes the presence of concentric cell layers moving more rapidly near the center of the vessel. A clear area of plasma occupied the periphery. White blood cells glided or rolled freely along as described by the Clarks<sup>24</sup> and were observed occupying the periphery of the stream.

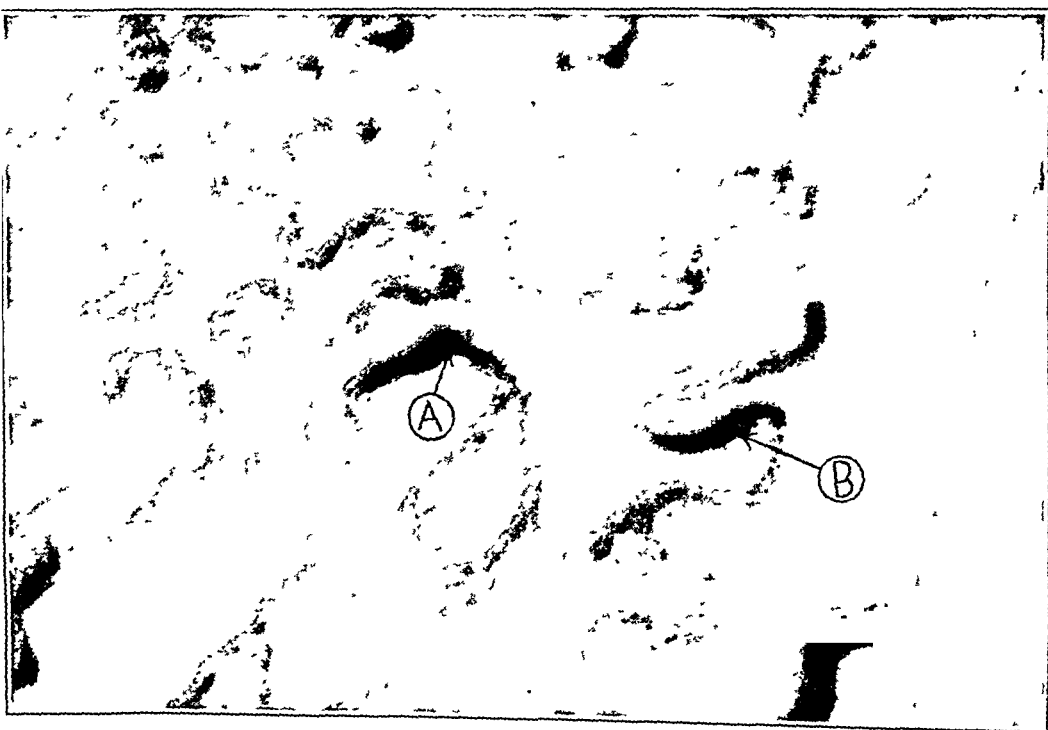


Fig 3—Normal circulation of capillary bed (slowed by partial occlusion of arterial flow for the photograph at one-fiftieth second exposure); capillaries 10 to 15 microns in diameter;  $\times 220$ . A, blurred streak of circulating discrete cells; B, vessel walls.

The smaller capillaries allowed red cells to flow smoothly in single file, demonstrating what Knisely has aptly termed "a perpetual bottle neck in the circulatory system." The rate of flow appeared to be slower in the longer capillaries. The red cells appeared to remain

<sup>23</sup> Krogh, A.: *The Anatomy and Physiology of Capillaries*, New Haven, Yale University Press, 1929, p. 5.

<sup>24</sup> Clark, E. R., and Clark, E. L.: Observations on Changes in the Blood Vascular Endothelium in the Living Animal, *Am. J. Anat.* **57**:385 (Nov.) 1935.

discrete, with no tendency toward clumping or rouleau formation. Knisely inferred from this fact that the erythrocytes normally repel one another.

2. *Local Trauma*.—In this phase of the study, the area of the vascular bed being traumatized was under continuous microscopic observation before, during and after injury. Experiments were conducted on 21 animals.

In all forms of trauma studied the vascular response was similar. With moderate changes in environmental temperature, such as inadequate control of the temperature of the Ringer solution, representing

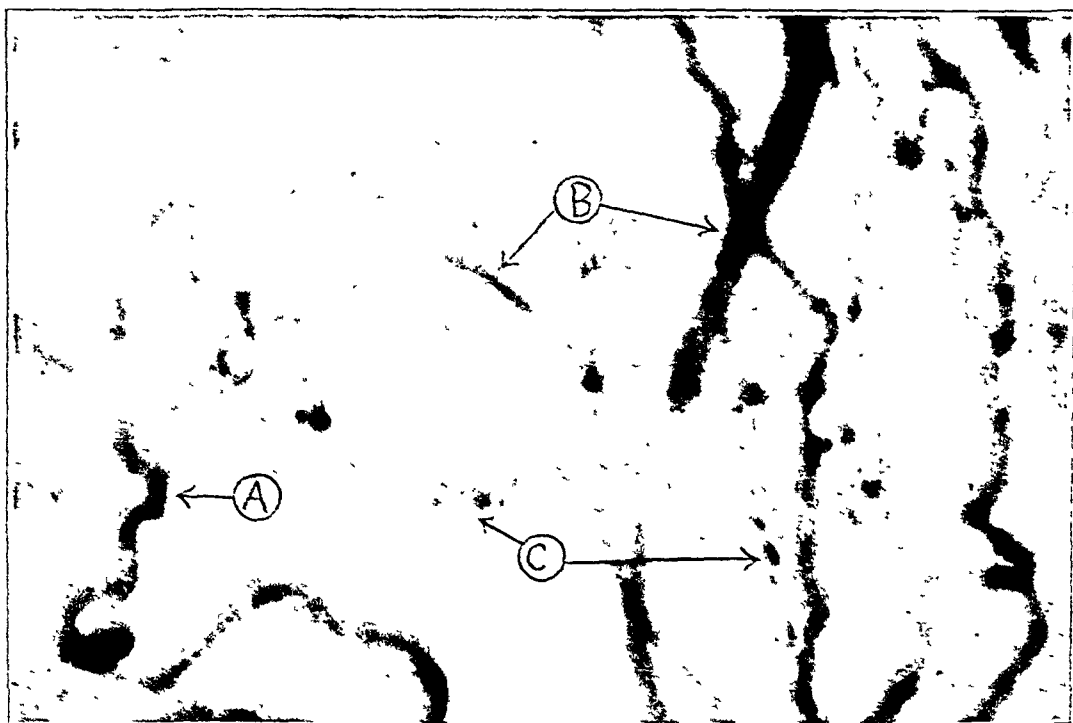


Fig. 4.—Local trauma:  $\times 150$ . *A*, static capillaries—dark red homogeneous columns of blood; *B*, flowing capillaries and venules—peripheral layer of plasma well shown; *C*, clumped erythrocytes at junction of static and flowing blood.

a minimal degree of trauma, slowing of the rate of flow occurred. This caused a granular appearance in the larger venules and arteries. This might progress to a very slow porridge-like flow, probably due partly to hemoconcentration and partly to red cell cohesion. Perivascular tissues showed evidence of varying amounts of edema. Many capillaries became static. White cells began to adhere momentarily to the injured endothelium and eventually became fixed in spite of continued flow in the vessel. This occurred earliest in the venous end of the capillaries. Diapedesis was observed, and these cells were

noted to pass into the tissues, as described by the Clarks.<sup>24</sup> In severer trauma the picture is predominantly one of rapid or instantaneous appearance of stasis.

Heat in the form of Ringer's solution at 80 C. produced stasis—that is, widespread immediate cessation of flow with apparent agglutination of erythrocytes into homogeneous dark red columns. With the continuation of the physiologic environment, resolution was observed in arterioles and venules and in capillaries at the periphery of the burned area. The first evidence of resolution was seen with the appearance of pulsation in some of the blocked arterioles, synchronous with the heart beat, and minutes later these vessels were cleared of their obstruction and blood was flowing. The capillary bed remained static until the conclusion of the experiment and for the most part was short circuited by arteriovenous shunts.

The application of Ringer's solution at 3 C. produced a similar picture, although resolution occurred in all vessels, including capillaries, within a few seconds.

Solid carbon dioxide caused an immediate cessation of flow which was resumed as soon as thawing occurred. After five to twenty seconds gradual slowing of the blood stream occurred, which progressed to stasis. Partial resolution occurred during the next two hours, with some capillaries remaining in a condition of stasis at the conclusion of the experiment. This reaction is similar to that observed by Quintanilla, Krusen and Essex,<sup>25</sup> who applied solid carbon dioxide to a Clarke window inserted into a rabbit's ear.

After crushing injuries to tissues, the same picture of widespread vascular stasis appeared. The manual manipulation or probing was very mild, such as could be produced during a gentle abdominal operation. The degree and rate of resumption of flow varied with the severity and duration of trauma.

Blalock,<sup>26</sup> in his studies of shock, reported: "The oxygen content of the blood from the femoral vein of a traumatized leg was high, while that of blood from the opposite extremity and head was low." He attributed the reduction in arteriovenous oxygen difference in the injured leg to "an accumulation of blood in the area traumatized, and unusual diminution in the amount of blood in other areas." We feel that such findings would be expected. The vascular stasis produced by trauma opens up arteriovenous shunts and allows the blood to pass

25. Quintanilla, R.; Krusen, F. H., and Essex, H. E.: Studies on Frost-Bite with Special Reference to Treatment and Effect on Minute Blood Vessels, *Am. J. Physiol.* **194**:149 (April) 1947.

26. Blalock, A., and Bradburn, H.: Distribution of the Blood in Shock, *Arch. Surg.* **20**:27-38 (Jan.) 1930.

into the venous circulation, without the usual reduction in oxygen content.

*Resolution of Stasis.*—At various intervals following trauma, in the vessels which had been blocked with columns of red cells flow was resumed. Careful observation of this process of resolution of stasis showed that in many instances at least, in which it was possible that one could observe the vessel at the moment of resolution, the red cells were no longer discrete but left the area and passed into the general circulation as clumps or aggregates of apparently agglutinated cells. Some of these agglutinated clumps contained only a few cells, whereas others, particularly those from larger vessels, were large masses that passed down the vein of exit like an express train. One could often observe the formation of these agglutinated clumps of red cells at a point where a freely moving vein joined one in a condition of stasis, as illustrated in a frame from the motion picture.

The resolution of stasis columns into discrete red cells, which pass as such into the general circulation, has also been observed. What factors determine the mode of resolution of vascular stasis are not known. The length of time that the vascular bed has been static may well be a factor in the production of agglutination.

Thus local trauma produced local stasis, and the breaking up of these static columns was observed. Agglutinated clumps of erythrocytes passed into the general circulation, henceforth to be identified as sludge.

In this study 21 animals were examined for the local effect of trauma. From a previously normal circulation, stasis was produced in each case and with all forms of trauma used.

3. *General Effect of Trauma.*—The presence of circulating clumps of agglutinated red cells has been observed in the general circulation in the past. It has usually been associated with disease states and trauma. This phase of study was devised to correlate by a controlled experiment the exact relationship between the local reaction to injury and general sludging of the vascular tree. Can these agglutinated red cell masses, formed at the site of trauma, be identified in the general circulation?

(a) Mild trauma (as described in "Methods") applied to two legs of the animal was not complicated by surgical shock, and the animals were active and ate well when they recovered from the anesthetic. Repeated observations of the conjunctiva and viscera were made, before and after trauma. On observation of the conjunctiva, the vascular bed appeared normal for two to four hours following injury, whereupon the earliest signs of abnormal circulation appeared. Blood

flow through the small vessels, particularly venules, became granular. In some capillaries the flow was in bursts or was intermittent because of partial or temporarily complete obstruction by agglutinated red cell clumps. Longer capillaries showed a series of clumps passing along, not unlike a string of beads. The narrow caliber conjunctival vessels showed early slowing and interesting reversal of the direction of flow.

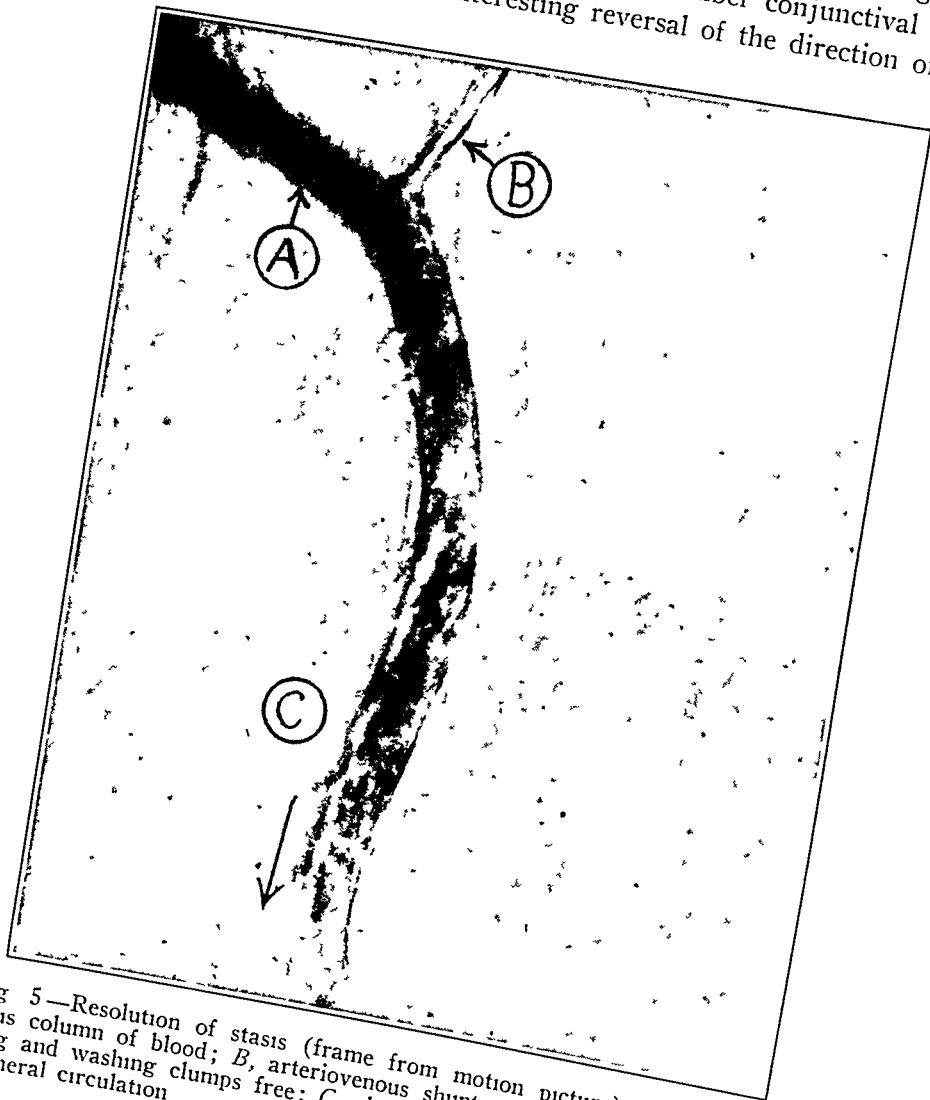


Fig 5—Resolution of stasis (frame from motion picture). *A*, static homogeneous column of blood; *B*, arteriovenous shunt in which the blood is rapidly flowing and washing clumps free; *C*, clumps flowing down draining venule into the general circulation

At twelve and twenty-four hours the generalized effect had progressed so that there were many metarterioles, capillaries and venules which were filled with red cells exhibiting no movement. This condition of stasis appeared to be a result of blockage by the circulating agglutinated masses or sludge.

Circulation in the large vessels was slower and the flowing material appeared granular. The conjunctiva was glistening and edematous, and at the twelve hour interval the surface was irregular, indicating a variation in the degree of edema. Several times elevation of the conjunctiva was observed directly over a capillary which had been suddenly occluded by a circulating clump. These observations were taken as evidence of generalized loss of fluid from the vascular tree, associated with the phenomenon of sludging. To support this concept, it is noted that Moon,<sup>27</sup> using an intravascular vital dye, observed evidence of generalized fluid loss in traumatic shock.

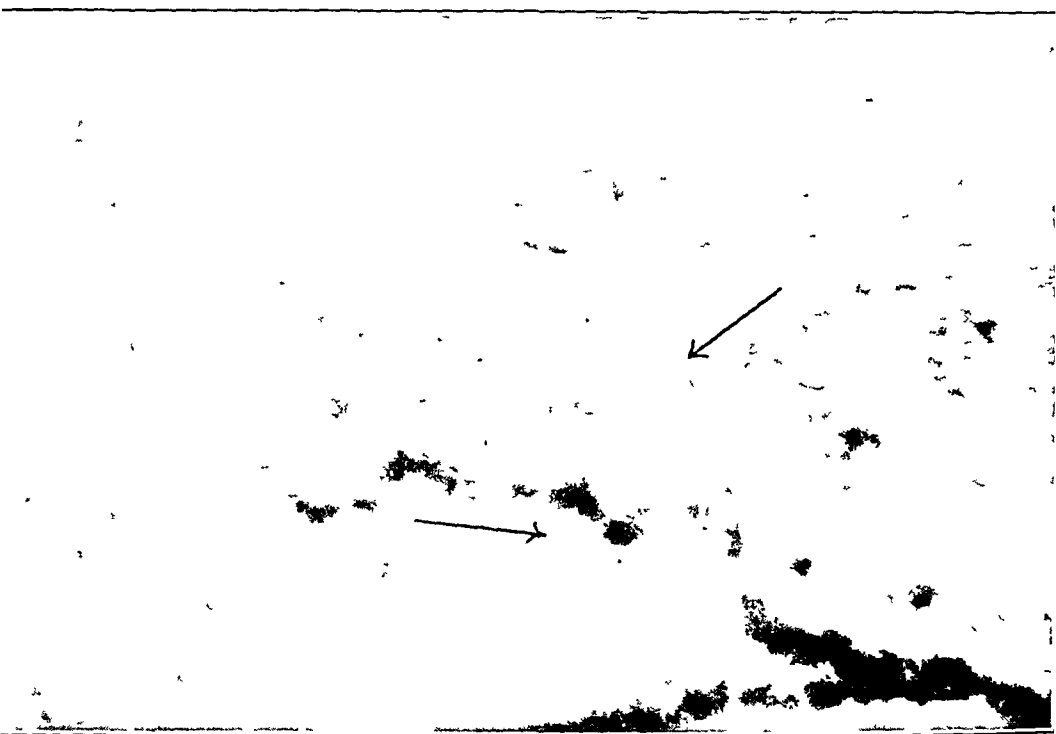


Fig. 6.—General effect of trauma (circulation slowed by partial occlusion of arterial flow for the photograph at one-fiftieth second exposure);  $\times 220$ . Circulating clumps flowing through capillary bed.

In five to ten days, most of the stasis had resolved, but there was still evidence of occasional agglutinated masses of red cells passing through the capillaries.

At some point in the experiment, the omentum and mesentery were exposed and examined, in order that the changes in them might be correlated with what had occurred in the conjunctiva. Here the thinner tissues permitted much clearer observations, higher magnifica-

27. Moon, V. H.: Shock: Its Dynamics, Occurrence and Management, Philadelphia, Lea & Febiger, 1942, p. 122.

tion and greater detail for photomicrography. The picture was somewhat different from that observed in the conjunctiva. Agglutinated masses were observed producing capillary bursts and intermittent flow, but in this mild trauma little or no stasis developed and the flow was more rapid. This is apparently due to the shorter and wider-calibered capillaries found in the portal system.

(b) Severe trauma (described in "Methods") was complicated by some degree of secondary shock with hemoconcentration. Of 20 dogs submitted to ten second burn, hematocrit determinations performed on 8 showed an average rise of 8 points, or 21 per cent increase over initial reading. Continuous recordings of blood pressure were made on 5 of 15 rabbits by means of a cannula in the carotid artery. All these showed a fall in blood pressure within one to two hours. Further details of this work will appear in a future publication dealing with shock.

Similar observations were carried out on the vascular bed remote from the area of trauma. The flow appeared abnormal in five to twenty minutes in all animals studied. The changes progressed with greater rapidity. The predominant feature was slowing, and stasis appeared to develop as a result of progressive slowing. In twelve and twenty-four hours definite circulating clumps could be observed in the slowly flowing blood, but their size and number were not in keeping with the degree of stasis present and suggested that the obstruction to flow had been produced by factors other than embolic blockage. Stasis was observed in both the conjunctiva and the omentum, and, once again, it was more pronounced in the former area. Edema developed in the conjunctiva. The loss of transparency in the omentum suggested the development of edema here.

The presence of general stasis has also been observed by Zweifach and Chambers,<sup>28</sup> while examining the living omentum in tourniquet shock experiments. Moon<sup>27</sup> has observed evidence of visceral capillary stasis in histologic sections taken from experimental shock experiments.

In the present study, the number of animals traumatized and the number in which sludging developed are shown in table 1.

It may be pointed out that in the severe forms of trauma, the slow, porridge-like stream which Knisely described as sludge, effectively camouflaged or made it impossible to determine the presence and size of circulating clumps. In the main, it was felt that clumps were present in all animals.

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28. Chambers, R.; Zweifach, B. W., and Lowenstein, B. E.: The Peripheral Circulation During the Tourniquet Shock Syndrome in the Rat, *Ann. Surg.* 120:791-802 (Nov.) 1944.



In sludge-free animals exposed to mild trauma without shock or significant hemoconcentration, agglutinated masses of red cells appeared in the general circulation consistently after injury. The stasis which resulted appeared to be due to blockage of capillaries by circulating clumps, was mild in degree and varied in different regions of the vascular bed.

In severe trauma a similar sequence of events occurred, but it was masked by hemoconcentration and shock, both of which can be major factors in the slowing of the circulation and stasis.

TABLE 1.—*Systemic Effect of Trauma*

Degree of Trauma	Animals		Number Showing Change			
	Dogs, No.	Rabbits, No.	In Conjunctiva		In Mesentery	
			Clumps	Stasis	Clumps	Stasis
A. Mild						
Burns.....	20	..	20	20	Not seen	
	..	10	10	10	10	0
Hammer blows.....	..	10	10	10	10	0
B. Severe						
Burns.....	20	..	20	20	Not seen	
	..	15	15	15	15	15

TABLE 2.—*Survey on 60 Human Subjects*

No. of Subjects	Degree of Agglutination and Stasis			Clinical Symptoms of Disease		
	Nil	Minimal	Moderate	Nil	Mild	Moderate
26.....	25	1	..	26	..	..
9.....	..	9	..	..	9	..
23.....	..	..	23	..	..	23
2 (discarded because of possible conjunctivitis)						

4. *Incidence of Agglutination of Red Cells in Human Subjects and Laboratory Animals.*—Examination of the conjunctiva for the presence of agglutination of red cells was made in 60 human subjects in an attempt to confirm Knisely's observations. Medical students, nurses, hospital employees and bed patients were studied.

The results are set forth in table 2. Moderate clinical symptoms included those of patients confined to the hospital with burns or frost-bite or convalescing from major operations. Mild clinical symptoms included head colds, sore throats, infected fingers and others.

It is interesting to note that only 1 of 26 apparently healthy subjects showed any degree of intravascular agglutination. Infections of the upper respiratory tract produced some degree of agglutination in almost

every case. There was a rough correlation between the severity of the illness and the degree of the agglutination. Two subjects who showed agglutination with abnormal flow were omitted because of possible conjunctivitis.

All experimental animals were examined initially as they came from the cages. Of a group of 88 rabbits, 49 were normal and 37 showed evidence of fine to moderate clumping, with various degrees of stasis. In one third of the latter, there was some obvious evidence of disease, such as subcutaneous abscesses, nasal discharge or diarrhea. On occasion all animals showed pathologic flow on several consecutive days, suggesting that the presence of a contagious disease among them was responsible for the clumping. In the last two winters it was

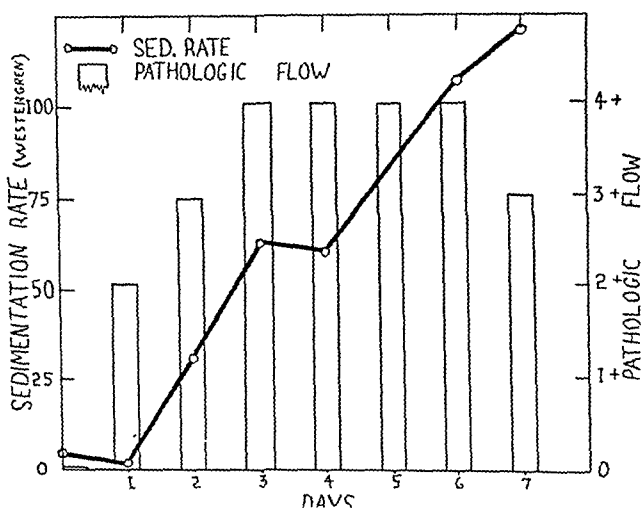


Fig. 7.—Relationship between sedimentation rate and pathologic flow. (Pathologic flow refers to a combined assessment of intravascular agglutination and vascular stasis.) A seven day study of 5 healthy dogs subjected to 6 per cent burn in boiling water for one to two seconds.

found necessary to discontinue work for periods of several weeks, because all the animals showed pathologic circulation.

Dogs from the cages showed a lower incidence of pathologic flow. Of 55 dogs, 39 showed normal circulation and 16 showed agglutination.

5. *Suspension Stability*.—Robin Fähræus' <sup>11a</sup> work on the relationship between suspension stability, or sedimentation rate, and intravascular agglutination has been confirmed in this study. Routine determinations of sedimentation rate were carried out on 20 dogs, fresh from the cages. Eleven were sludge free, and with 1 exception all had sedimentation rates below 10. Of the 9 showing circulating clumps of red cells, all had sedimentation rates ranging from 10 to 100. The sedimentation rate appeared roughly to parallel the degree of agglutination.

Sedimentation rates were followed on 30 burned dogs. These were selected animals, with normal-appearing circulation and sedimentation rates within normal limits. After the burn, intravascular agglutination of red cells and vascular stasis were observed in all animals within one hour. The sedimentation rate, however, decreased during the first twenty-four hours and then rose to very high levels. Five of these dogs were followed for seven days, and the results are illustrated graphically (fig. 7). This temporary lack of correlation between sedimentation rate and pathologic flow may be attributed to other factors which are already known to influence suspension stability, such as



Fig. 8.—Histologic section showing normal liver sinusoid. *A*, Kupffer cell—no phagocytosis; *B*, discrete free red cells. Hematoxylin and eosin;  $\times 2,100$ .

hemoconcentration, protein content of the plasma or alteration of temperature, hydrogen ion concentration and electrolytes.

*6. Fate of Agglutinated Cells.*—Coincident with the healing of traumatized tissue, the circulation returns to its former state. Whether the blood undergoes deagglutination or whether the clumps are phagocytosed by the reticuloendothelial system we do not know. Whether or not the ingestion of the clumps of red cells represents the fate of all or only some, such a process would serve as a possible explanation of the anemia that follows trauma.

Knisely<sup>21</sup> has observed the ingestion of coated foreign particles by the phagocytes of the liver in living frogs. He has suggested—but

not reported—that Kupffer cells may ingest the agglutinated clumps of red cells, because of a fibrin-like coating similar to that covering the foreign particles. At autopsy of 27 dogs performed twenty-four hours after both severe and mild burn, all showed enlargement and marked engorgement of the liver.

The liver has been transilluminated and observed at intervals in normal rabbits and after burns. A reasonably good view of the sinusoid circulation was obtained and photographed. Immobilized masses of red cells were observed on occasion, and it was reasonable to suspect that they were ingested clumps which had been produced



Fig. 9.—Histologic section of liver sinusoid from traumatized animal. Kupffer cell distended, with two red cells in its cytoplasm. Hematoxylin and eosin;  $\times 2,100$ .

by the burn. Pathologic sections of liver taken at intervals of three hours to eight days following burns were compared with the normal. Hematoxylin and eosin and prussian blue stains showed evidence of phagocytosis of intact red cells in 5 livers from 15 burned animals. A similar study as a control indicated the presence of phagocytosis in 1 liver among those taken from 5 normal animals. These histologic observations were made by Dr. S. Bensley, who was not aware of the nature of the section under examination.

7. *Vascular Stasis*.—This term has been used in the historical outline and throughout our observations to denote complete cessation of flow in vessels as a result of trauma. We have already concluded

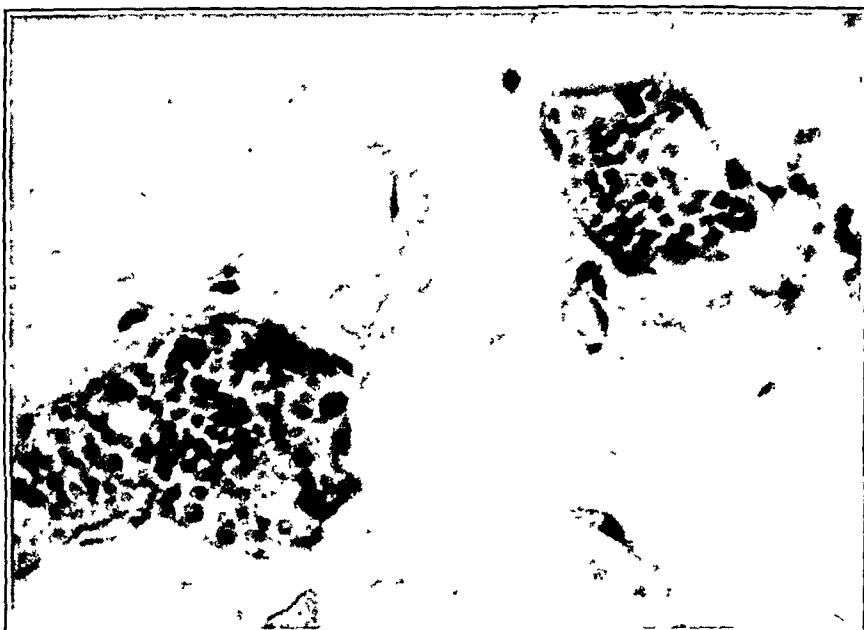


Fig. 10.—Section of normal subcutaneous tissue; discrete red cells in venule. Hematoxylin and eosin;  $\times 440$ .

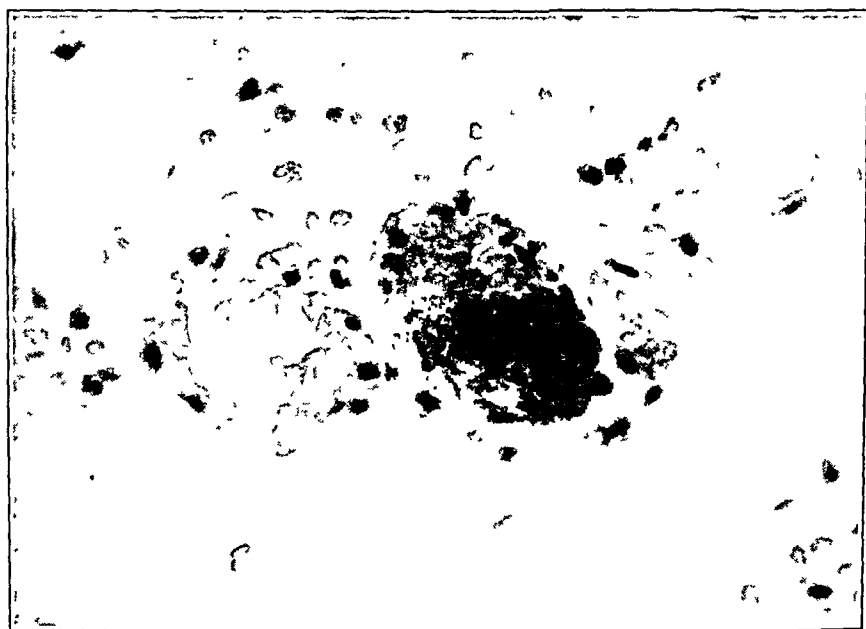


Fig. 11.—Section of subcutaneous tissue after burn to adjacent skin. The red cells are closely packed and probably appeared as a dark red homogeneous mass before fixation of tissue. Hematoxylin and eosin;  $\times 440$ .

that this invariably takes place and that the extent of the stasis and the time taken for resolution depend on the extent and duration of the injury.

In an attempt to correlate these observations with the pathologic picture, sections were taken of skin and muscle of the burned and hammered extremities of dogs and rabbits studied. These showed the familiar picture of capillaries and larger vessels packed with red cells. Most American pathologists describe this as congestion or hyperemia and incorrectly imply thereby that there is still flow present. It is interesting to note the divergence of opinion that exists between European and American pathologists on this fundamental reaction of tissues. Further confusion is added by the popular American interpretation of the word stasis as meaning slowing of the circulation.

In this study vascular stasis has also been observed in areas remote from the region traumatized. In injury uncomplicated by hemoconcentration or shock, this stasis was considered due to embolic blockage of vessels by agglutinated clumps of red cells. Observations on shocked animals suggested that vascular stasis could be produced by hemoconcentration or slowing of the stream induced by shock. We should therefore like to postulate five important causes of vascular stasis associated with trauma: (1) local reaction to injury, (2) embolic blockage, (3) hemoconcentration, (4) reduced hydrostatic pressure (shock) and (5) vasoconstriction.

It would appear difficult or impossible at the present time definitely to identify vascular stasis on pathologic section. This is no doubt due to the series of dehydrating chemicals to which tissues are exposed before they reach the slide. When photomicrographs of normal skin and that taken twenty-four hours following a burn are compared the latter shows what pathologists have described as congestion. Our studies would indicate that vascular stasis existed in the burned skin, but these slides are difficult to interpret and do not clearly demonstrate the process seen in vivo.

#### COMMENT

The nonspecific nature of the physiologic processes of intravascular agglutination of erythrocytes and vascular stasis is evident. It is apparently linked with coagulation of blood and influenced by the many changes which occur in the blood's colloid and electrolytic states. Many obvious questions arise:

1. *What causes vascular stasis in local reactions to injury?*—Is it due entirely to leakage of fluid with silting of red cells, or is there a physical-chemical alteration of the state of the blood which causes local agglutination? We observed evidence of fluid leak, but we

have also sometimes observed the resolution of the stasis column into agglutinated clumps of red cells. In support of the latter theory, we have observed an increased susceptibility to vascular stasis in animals already showing a degree of generalized intravascular agglutination.

2. *Are the agglutinated clumps of red cells formed only in the traumatized area, or is there a chemical alteration in the blood which induces a generalized clumping throughout the vascular tree?*—Agglutinated clumps of red cells have been observed leaving the traumatized area. Whether or not they represent the sole source of clumps following injury is not known. Since reduced suspension stability is a generalized reaction on the part of the blood, one might suspect that both factors are in operation.

3. *Should the term "sludge" be used to denote the presence of agglutinated clumps of red cells slowing the circulation, or should it include the slow porridge-like flow seen with hemoconcentration and shock?*—Knisely has used the term "sludge" to denote all the microscopic circulatory changes following trauma (and disease). He described generalized retardation of flow by agglutinated clumps of red cells with subsequent stasis. He has not clearly indicated that a similar picture, with generalized vascular stasis, can be produced in severe burns or traumatic shock very early and before many agglutinated clumps have entered the circulation. This very early picture appears to be one of low blood pressure and hemoconcentration from loss of fluid at the site of injury. The latter concept will be clarified in a paper to follow.

4. *Is vascular stasis an important cause of tissue anoxia and resultant tissue death following local trauma?*<sup>29</sup>—This question is to be dealt with in a later paper.

5. *Is the process of erythrocyte agglutination a factor in the production of shock?*—It would appear to be a cause of generalized fluid loss following injury and thus could add to the loss of circulating blood volume. It is well known that the fatal volume of local fluid loss from trauma is less than the fatal volume of loss from hemorrhage. This constitutes a possible explanation of the discrepancy.

6. *Is the extension of vascular stasis the origin of red clot formation in phlebothrombosis?*—This would appear to be a natural sequel to stasis, but until there is a means of identifying stasis and thrombosis pathologically it will probably remain unanswered. There is

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29. Bigelow, W. G.: The Modern Concept and Treatment of Frost-Bite, *Canad. M. A. J.* **47**:529-534 (Dec.) 1942. Kreyberg and Rotnes.<sup>18</sup>

very probably an important time factor related to the reversibility of stasis.

7. *Could embolic blockage of kidney cortex by agglutinated red cells be a factor in the production of traumatic anuria, or the "crush" kidney?*—Trueta was interested when it was suggested to him that cortical vessels could become static from embolic blockage by circulating clumps. This type of production of stasis with the opening of arteriovenous shunts, as he described in his work on the "crush" kidney, is typical of the vascular response seen in all tissue studied.

8. *Could phagocytosis of the agglutinated red cells be a cause of secondary anemia following burns?*—This has been already discussed. A further explanation might be that there are diminished erythropoietic properties of the red marrow as a result of the embolic effect of the circulating clumps.

9. *Is the process of erythrocyte agglutination a beneficial reaction in trauma?*—This is an intriguing question and will probably not be answered until the deagglutinating agent has been found. The previous questions suggest that in advanced degrees this is a deleterious process, but it may be found eventually to be beneficial.

These and many other questions which arise are as yet unanswered and indicate the need for further study.

#### SUMMARY

1. Observations and microscopic cinema recordings were made on the living vascular bed in health and in reaction to trauma. An attempt was made to clarify the meaning of the terms vascular stasis and sludge.

2. The methods of study described made it possible to maintain the living vascular bed in its normal physiologic state for four hours.

3. Normal blood flow was smooth and regular, with no tendency for erythrocytes to agglutinate. There was no vascular stasis, and the sedimentation rate was usually below 10.

4. After local trauma to the area under microscopic observation, there was cessation of flow in the smaller vessels. The red cells became packed into dark red homogeneous masses. This phenomenon has been described as vascular stasis. Resolution of stasis was observed, in which the columns often broke off into the general circulation as circulating clumps.

5. Animals exposed to trauma consistently showed agglutinated clumps of red cells in the general circulation after injury. These clumps appeared to act as emboli and produced stasis in areas remote from the trauma.



6. In trauma followed by shock, hemoconcentration and reduced rate of flow complicated the picture.

7. It was difficult to correlate the picture of stasis seen in vivo with that seen in histologic sections.

8. Possible clinical applications of the phenomenon are discussed.

9. Microscopic cinema recordings have been made in color to demonstrate each phase of the study.

Prof. R. M. Janes, head of the department of surgery, and Mr. Walter Cowan, senior technician, cooperated in this study. Dr. Sylvia Bensley, of the department of histology, interpreted the histologic sections.

Department of Surgery, University of Toronto.

### DISCUSSION OF PRECEDING PAPERS

DR. JOHN H. OLWIN, Chicago: I should like to comment very briefly on Dr. Lillie's paper concerning the prevention of pulmonary embolism—that is, regarding the methods for the control of anticoagulants, particularly dicumarol.<sup>®</sup> I agree that the early use of heparin, before dicumarol<sup>®</sup> becomes effective, is very important. Dr. Lillie mentioned that in certain instances thrombi developed after the patient had been on anticoagulants. I believe that a certain percentage of these, perhaps a large percentage, is the result of an inadequate control of the anticoagulant effect. Dr. Quick's method, which is used rather universally, does not take into account a large number of variables in the coagulation process and may give a false prothrombin reading as a result of the overactivity or underactivity of one or more of them. On the other hand, the two stage method, which was devised by the group at Iowa City and which is not well enough known, controls these factors and, for the most part, measures only the prothrombin level. In a series of cases which we have followed with the use of the two stage method we have been able to reduce the prothrombin to a therapeutic level and maintain it there rather uniformly, which we have been unable to do with the Quick test run in parallel with the two stage test. The latter method has two particular advantages: First, it is much safer because it does not allow the patient's prothrombin to drop to a hazardous bleeding level without the knowledge of the person who is controlling the therapy. Second, if bleeding does occur, it is usually slight and because the patient's prothrombin level is not far below the bleeding threshold it is often unnecessary to use heroic measures to bring the prothrombin back to a safe level, and hence the therapeutic effect is not disturbed.

If the two stage test is used more universally, I believe that results with anticoagulants will be materially improved.

DR. LOUIS G. HERRMANN, Cincinnati: At the Cincinnati General Hospital the conservative amputation of gangrenous toes has been practiced for over fifteen years. We are entirely in accord with what Dr. Regan has said about the reduction in mortality and loss of limbs in patients with gangrene or localized infection in the joints of the feet. The presence of a gangrenous toe in a diabetic patient is no longer an absolute indication for a supracondylar amputation. It has been our experience, however, that the transmetatarsal type of amputation gives a much better weight-bearing foot than simple removal of the toes, especially when the first metatarsophalangeal joint is destroyed by gangrene or infec-

tion. I want to emphasize the fact that in performance of the operation the tendons must be anchored in their sheaths by transfixed sutures of fine chromic surgical gut before they are cut. Some failures have been due to retraction of these tendons, especially the extensor tendons of the toes, with spread of the infection up the tendon sheaths. Transmetatarsal amputations of this type give good functioning stumps which do not require special prosthesis for normal weight bearing and locomotion. It is important to save as much plantar skin as possible, so that the end of the stump will be partly covered by the thick plantar skin when healing and contraction of the stump takes place. The dorsal part of the end of the stump is usually covered by small split thickness skin grafts after a good granulation tissue base has developed.

Our experience supports the belief and experience of Dr. Regan and his associates that many legs can be saved and made useful again even when one or more toes are gangrenous. Stimulation of the arterial circulation and the use of antibiotics and chemotherapeutic agents have greatly lessened the risks of conservative amputations, even in the face of infection in a diabetic patient.

I should like to ask Dr. Lillie whether it is the policy at the University Hospital suddenly to discontinue use of anticoagulant drugs in the management of venous thrombosis. We have found that there is a sudden rise in the coagulability of the blood when anticoagulants are discontinued abruptly. Some of the so-called recurrences of venous thrombosis after adequate periods of anticoagulant therapy may be due to this peculiar phenomenon. I should advise use of small doses of heparin or dicumarol<sup>2</sup> for three to four weeks after all signs and symptoms of venous thrombosis have subsided and the patient is normally active again as the best means of preventing sudden recurrence of venous thrombosis.

DR. WALTER W. CARROLL, Chicago: I wish to commend the author of the paper on hernia and should like to bring up merely one point. I also favor early ambulation, but fair evaluation of the vascular complications must include a more complete consideration of the patient's activities prior to hospital admission, as well as of his inactivity as a result of the anesthesia. Of course, patients have been known to rest in bed at home before coming to the hospital. On the other hand, it is equally possible to discover that a patient has been exercising strenuously before entering the hospital, with the possible formation of a spontaneous clot in one of the small veins of a leg. Such patients will confuse the statistics. In addition, when a patient is under spinal anesthesia or general anesthesia for some time (perhaps the anesthesia lasts only two hours, yet the patient lies quietly another four hours in bed) a venous clot may form from such inactivity.

I should like to commend Dr. Collier's representatives on their feeling about anticoagulants. It is obvious that you will find out in a minute or two that I have a deep prejudice, built on enthusiasm perhaps, against femoral ligation and in favor of anticoagulants. Some of the 7 deaths in this series might have been averted if the anticoagulants had been applied routinely to that group. It was interesting to note that there were no deaths in the group receiving anticoagulants.

In reference to Dr. Szilagyi, one might conclude that such a study could arise from a feeling that we have to defend the concept of femoral vein ligation by pointing out the absence of sequelae in the lower leg. Three months is not enough time to use as a measuring stick for follow-up of femoral vein obstruction. Bauer and his group of Swedish clinicians, with one of the best controlled studies on possible phlebitis sequelae, have shown that one to two years follow-up is more complete. In support of the use of anticoagulants in phlebothrombosis, they made the very pertinent point that in the beginning the clot is located in one of the vena comites, distal to the popliteal junction. The reason that the anti-

coagulants do so well is that clotting is prevented in all the other parallel branches and normal collateral return is not mechanically impeded. Not only is it the migration of the clot that we are concerned with but also the sequelae. If the anticoagulants are used, we will tend to keep many venous channels open for the return flow. Femoral vein ligation, of necessity, produces occlusion and obstruction of return flow.

DR. J. SUTTON REGAN, Buffalo: I should like to state that a number of patients who have just the one large toe remaining think that their balance is aided by it. At least it does not seem to impair their walking ability. The big point that I should like to make today is that we have reduced our high amputations from 70 per cent to 18 per cent, and a number of people have useful legs, which formerly would have been amputated.

DR. JOHN H. POWERS, Cooperstown, N. Y.: If I have left with the discussers of my paper the impression that I do not favor early ambulation, I have been grossly at fault. In my opinion, early postoperative activity has everything to recommend it and nothing to condemn it. I wish to impress on this audience, however, that many of the reports in the literature about the decrease to the point of nonexistence of vascular complications among patients who have been permitted early postoperative activity are not in accord with my own experience. I have read papers, as you no doubt have, by surgeons whom many of us know, stating that they have operated on 1,500 patients, 2,000 patients or 10,000 patients with not a single instance of postoperative thrombosis when ambulation has been allowed on the first postoperative day. Gentlemen, that does not happen. Thrombosis in the deep veins of the legs is not only not eradicated by prompt postoperative activity, but the frequency of this complication is unaltered by early ambulation. As for remaining in bed or going on a spree in preparation for operation, I live in a rural area where the patients have no time to stay in bed and no money to spend on bibulous holidays before reporting for hernioplasty. In fact, most of them do their evening chores, enter the hospital the next morning, have their hernias repaired the following day and go home from three or four days to seven or eight days afterward. They are back milking the cows two weeks from the day they were operated on.

DR. R. H. LILLIE, Ann Arbor, Mich.: Certainly we have something to gain from Dr. Olwin's first observation, that our control of the prothrombin levels in patients treated with anticoagulants is far from perfect. We attempted to report here what our experience has been in the past, and that includes the first patients to whom we gave anticoagulants. I believe our complications are being diminished, especially as far as hemorrhage is concerned, and perhaps the thing that is going to help most is a better test to follow the prothrombin levels. However, I should like to say—repeating myself somewhat—that patients' sensitivity to anticoagulants, particularly dicumarol,<sup>®</sup> is not uniform, and in spite of following the level daily or oftener, two individual patients may have quite different responses to the same dosage, and the level may be quite rapidly changed in one patient by what would be a moderate dose for the other. In regard to the second question, I think we certainly agree that heroic methods are not at all necessary if the prothrombin level falls to what would be considered a dangerous level if allowed to persist. When it is between 10 and 20 per cent, we discontinue further administration of dicumarol,<sup>®</sup> but this does not necessarily mean that one must resort to massive doses of vitamin K or blood transfusion to bring up the patient's prothrombin concentration. In our experience, when a low level is noted on one determination, dicumarol<sup>®</sup> is discontinued, and the prothrombin concentration will

usually rise automatically in sufficient time to prevent bleeding. In regard to Dr. Herrmann's question, "Is it policy to discontinue anticoagulants quickly?" I think that he has in mind the raising of prothrombin concentration suddenly. The anticoagulants are discontinued in the usual case of venous thrombosis after a period of ten days. The patient is allowed to regain normal prothrombin concentration, and if he is ready to go home we frequently resort to an amount of vitamin K sufficient to bring the patient's prothrombin concentration to 50 per cent, which we would consider a safe level to allow the patient to leave the hospital if he is not going to take any more dicumarol.<sup>6</sup>

D. D. EMERICK SZILAGYI, Detroit: Dr. Carroll has stated that we are partial to ligation of veins. I should like to point out that while he, by his own admission, professes prejudice against such ligation, we are definitely not prejudiced against the use of anticoagulants. As to the remark that our statistics are not entirely valid since serious sequelae commonly occur after three or more months of freedom from trouble following ligation, I must say that I am unaware of any account in the literature that would bear out this point. The statistics of Swedish investigators, in particular those of Gunnar Bauer to which Dr. Carroll refers, did not concern postligation cases. They dealt with medical and postoperative thrombophlebitis treated with heparin. The cases with serious sequelae described in these studies were all neglected ones of long standing, and they are in no way comparable to those of our series. Our patients were closely watched, as mentioned in our paper, for periods varying from one month to seven years, and we can say with assurance that if a patient had no sequelae at the end of three months, he had no sequelae at the end of any further period of observation provided he obeyed a few simple rules in the care of the affected limb.

It was not our purpose in our presentation to prove the superiority of one method over another or to establish criteria for the application of either form of treatment. As a matter of fact, the exclusive use of either method is unwise. There are cases in which ligation is the better choice; anticoagulants, now becoming increasingly more popular, must be given preference in other cases. In this series we have limited ourselves to the use of vein interruption mainly for the purpose of evaluating the method in general and to observe its effects on the limb. No doubt, in the future a balance will be struck and the indications for each method will be clearly defined. In the meantime, I think it is a useful undertaking to attempt to find out what one may expect in the evolution of the changes that ligation brings about in the affected limb.

## BIOPSY OF DIFFUSE PULMONARY LESIONS

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**D**IFFUSE, extensive, bilateral pulmonary lesions producing minimal symptoms and frequently found on routine roentgen examination present a challenging diagnostic problem. They may represent a fibrotic reaction to inhalation or radiation trauma or to infection, both bacterial and fungus; a primary pulmonary neoplasm, or metastatic lesions from asymptomatic primary carcinoma elsewhere. A presumptive diagnosis can occasionally be made on the basis of the history; examination of bronchial fluid, blood and bone marrow; sensitivity studies, or biopsy of peripheral lymph nodes. An absolute diagnosis, however, cannot be made in a large number of patients by these indirect methods. In a series of 50 patients we have been able to diagnose such lesions with certainty by the use of a simple technic of pulmonary biopsy, which in our experience has led to no serious complications and has been of minimal discomfort to the patients.

### SURGICAL TECHNIC

In the first 12 cases in which pulmonary biopsy was done, endotracheal anesthesia with pentothal sodium®-curare induction was used; however, because of occasional bronchitis and laryngitis observed in these patients, cyclopropane-oxygen delivered under positive pressure with a face mask is the form of anesthesia now in use. Since the biopsy specimen is taken from the inferior border of a lobe, we have found an anterior incision in the third or fourth intercostal space on the right to be most advantageous, this approach giving access to the inferior margin of the upper, middle and lower lobes.

The surgical procedure is illustrated in figure 1. After routine preparation of the skin with the patient in a supine position an 8 cm. incision is made over the fourth anterior intercostal space, beginning

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From the Department of Research Surgery, the Ohio State University.  
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4 cm. from the lateral border of the body of the sternum (fig. 1, 1). In women the incision is made submammary, and upward retraction of the breast is used to expose the third or fourth intercostal space. After separation of the fibers of the pectoralis major and minor muscles, the intercostal space is exposed and the intercostal muscles cut midway between the margins of the ribs. The blades of a medium-sized Richardson retractor are inserted parallel with the ribs into the incision and when the handles are rotated 90 degrees outward spreading of the ribs occurs, with adequate exposure of the interlobar fissure (fig. 1, 2).

With slight increase in the intrabronchial pressure by the anesthetist, the lower margins of the upper, middle or lower lobes will herniate

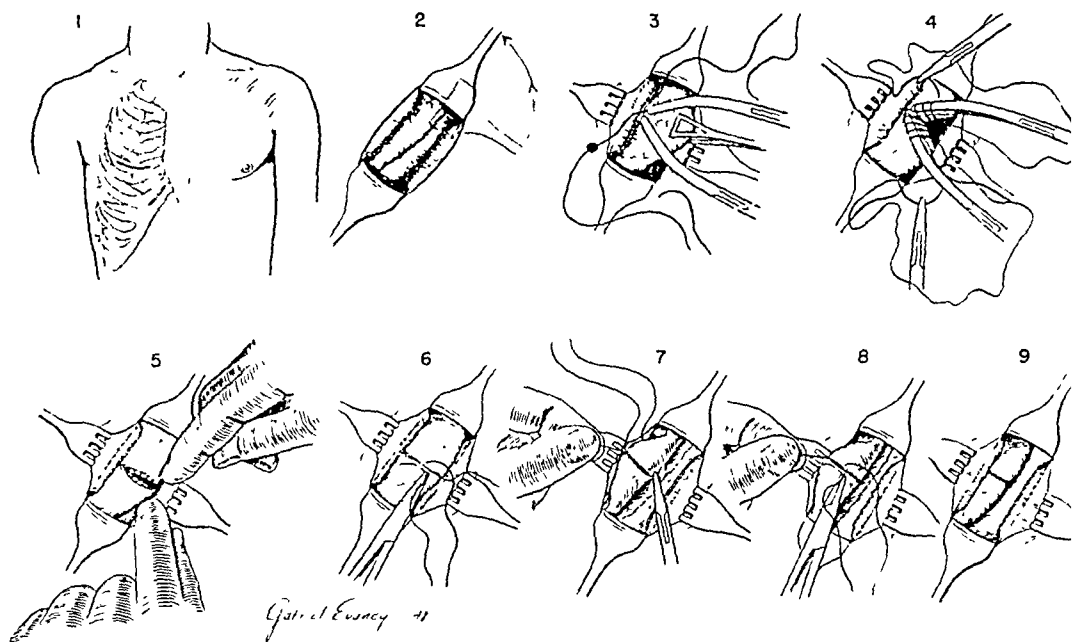


Fig. 1.—Technic of pulmonary biopsy.

through the incision. A small Duval lung clamp is used to grasp the edge of the lobe at the proposed site of the biopsy. A mattress suture of 000 chromic surgical gut with a swaged curved needle at each end is placed at the apex of the biopsy site 2 cm. from the margin of the lung. Two Carmalt hemostats are now applied with the tips approximating the placed mattress suture, isolating a wedge of pulmonary tissue, which is now sectioned and removed (fig. 1, 3).

The two ends of the suture are now run down as an over and over stitch to the periphery of the lung on each side (fig. 1, 4). The Carmalt clamps are removed, the suture pulled tight and the two ends tied to bring the cut surfaces together (fig. 1, 5). One end of the suture is used as a continuous Cushing stitch to appose the visceral pleural



Fig 2 (case 1).—*A*, roentgenogram, and *B*, photomicrograph of Boeck's sarcoid



Fig. 3 (case 2).—*A*, roentgenogram, and *B*, photomicrograph of fibrocascous tuberculosis.



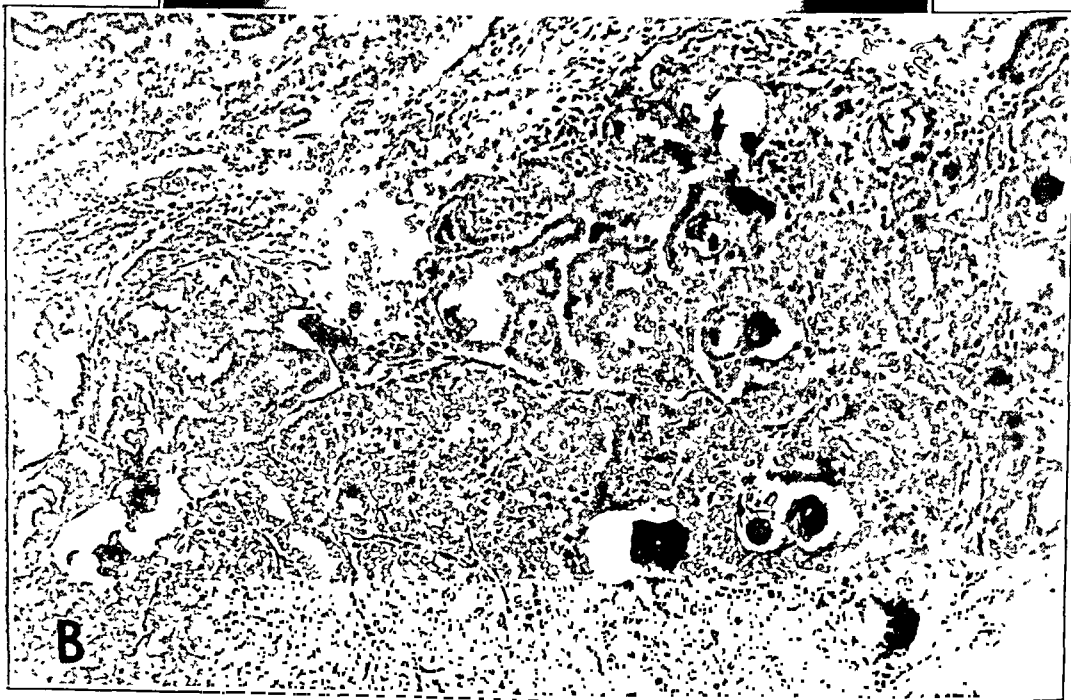


Fig. 4 (case 3).—*A*, roentgenogram, and *B*, photomicrograph of pulmonary metastasis from thyroid carcinoma.

surfaces, first on the superior surface (fig. 1, 6) and, after transfixion at the site of the first mattress suture, back to the edge of the lobe on the inferior surface (fig. 1, 7 and 8). The suture is now tied and cut. The suture produces hemostatic and air-tight closure (fig. 1, 9).

A 14 F. catheter is placed into the pleural space, and the wound is closed by suturing the intercostal muscles with 00 silk, approximating the pectoral muscles and again suturing the skin. Because of the constant positive pressure anesthesia there is no necessity for the removal of air; however, 5 cc. of saline solution containing 100,000 units of penicillin is instilled into the pleural space and the catheter withdrawn. No post-operative drainage is used. The patient is allowed out of bed on the day of operation and is usually discharged on the third postoperative day.

#### REPORT OF CASES

CASE 1.—M. S., a 56 year old white railroad clerk, entered the hospital with the complaint of fatigue, dyspnea and pronounced loss of weight over a period of two years. A diagnosis of pulmonary carcinomatosis had been made elsewhere and radioactive isotope therapy recommended. Roentgenograms (fig. 2A) showed marked increased density in the hilar regions with irregular densities extending into the periphery of both lungs. Thorough examination of the patient failed to show the presence of a primary malignant tumor. Bronchoscopic examination showed nothing significant. Pulmonary biopsy revealed the lesion to be Boeck's sarcoid (fig. 2B). The patient returned to his regular occupation and has shown no progression of the lesion.

CASE 2.—R. B., a 38 year old Negro laborer, was admitted to the University Hospital for investigation of productive cough, pain in the chest and progressive dyspnea of nine years' duration. Roentgenograms (fig. 3A) of the chest revealed a diffuse hazy infiltration predominating in the lower pulmonary fields. Repeated examination and cultures of the sputum and bronchial aspirations were negative for acid-fast bacilli. The tuberculin and histoplasmin tests elicited negative reactions. Pulmonary biopsy revealed fibrocaceous tuberculosis (fig. 3B). The patient had an uneventful postoperative course.

CASE 3.—W. V. G., a 12 year old white boy, was admitted to University Hospital in severe respiratory distress due to tracheal compression by a thyroid tumor, first observed four weeks previously. Tracheal decompression was accomplished by partial resection of the tumor, which was found to be a thyroid carcinoma. Roentgen examination of the chest (fig. 4A) showed multiple miliary, fairly discrete densities in both lungs, apparently representing metastasis from the thyroid carcinoma. Radical resection of the primary tumor was not performed when pulmonary biopsy confirmed the roentgen diagnosis of pulmonary metastasis (fig. 4B). There has been regression of the lesion following radioiodine therapy.

CASE 4.—H. M., a 34 year old white nurse, entered the hospital with the complaint of a dry cough associated with a low grade fever of about four months' duration. Roentgen examination (fig. 5A) revealed a diffuse flocculent infiltration in the lower portions of both lungs. On repeated examinations sputum and gastric washing were negative for acid-fast bacilli. Boeck's sarcoid was suggested by the roentgenologist as a diagnostic possibility, and in the absence of enlarged peripheral lymph nodes a pulmonary biopsy was performed. When a metastatic

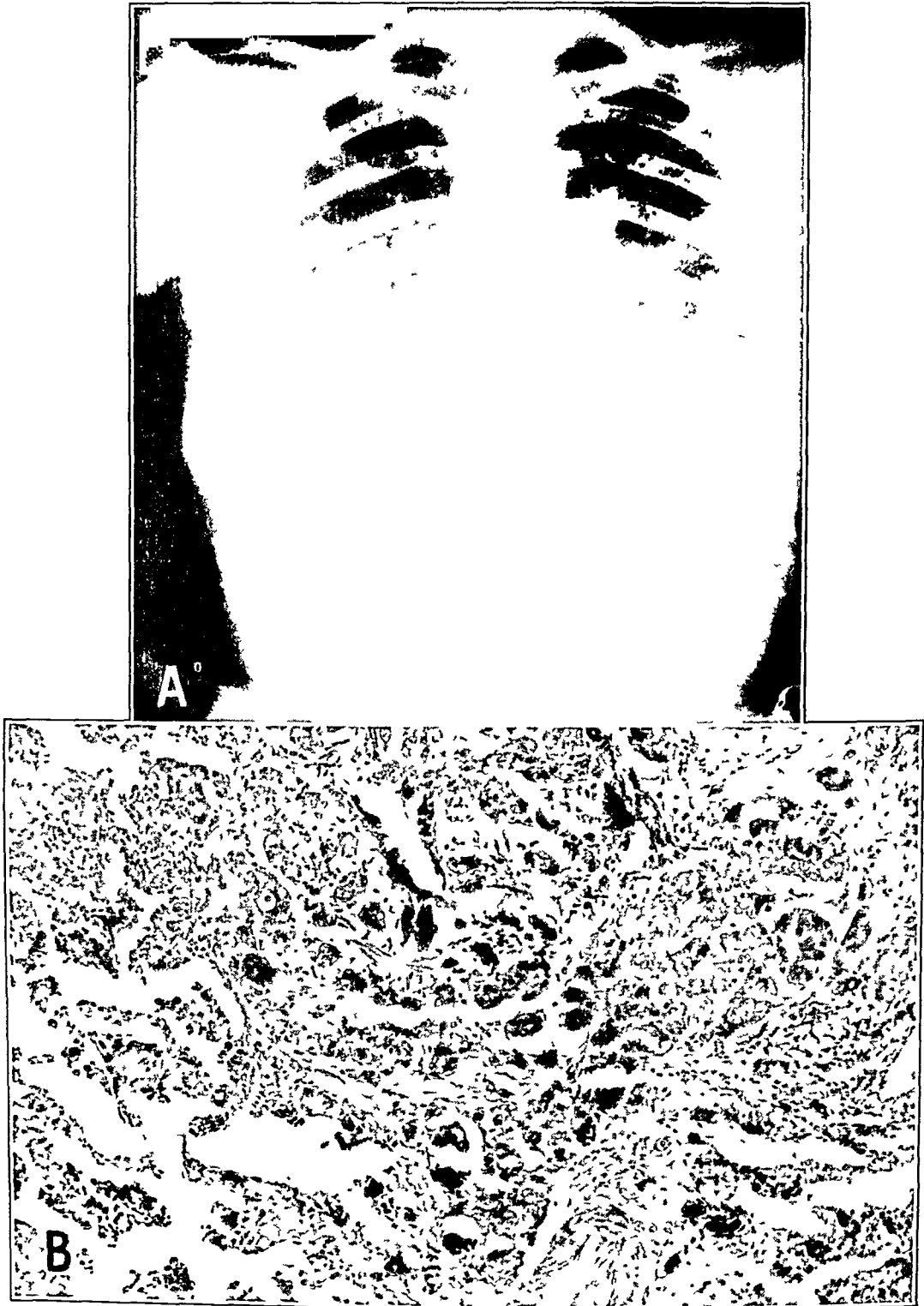


Fig. 5 (case 4).—*A*, roentgenogram, and *B*, photomicrograph of pulmonary metastasis from adenocarcinoma of breast

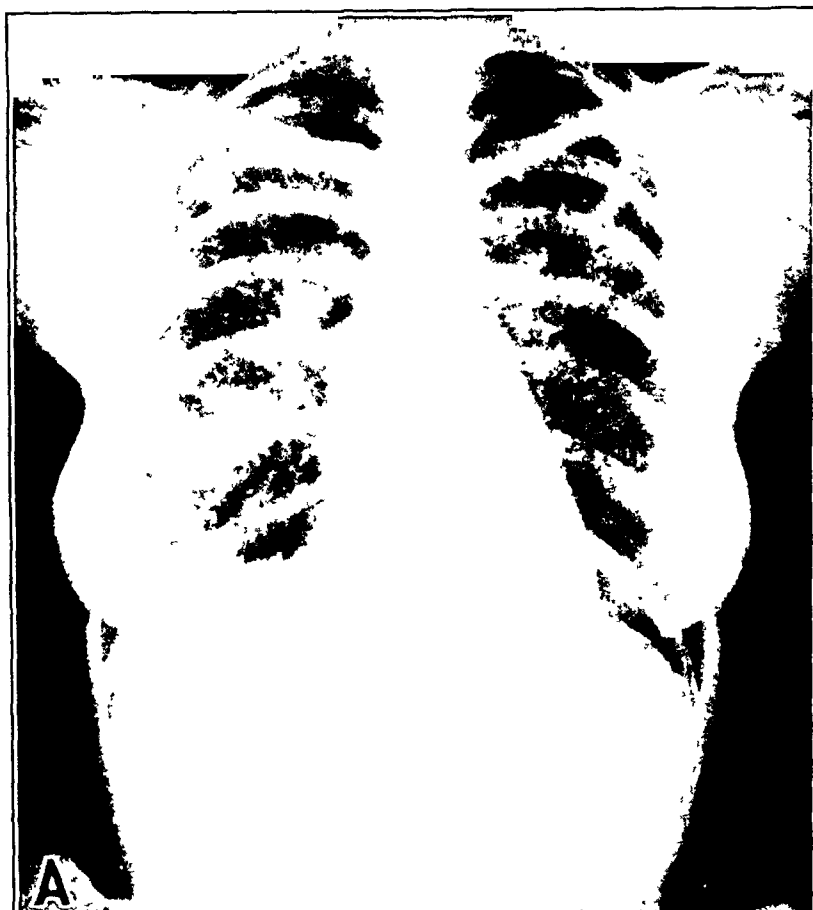


Fig. 6 (case 5).—*A*, roentgenogram, and *B*, photomicrograph of Boeck's sarcoid.

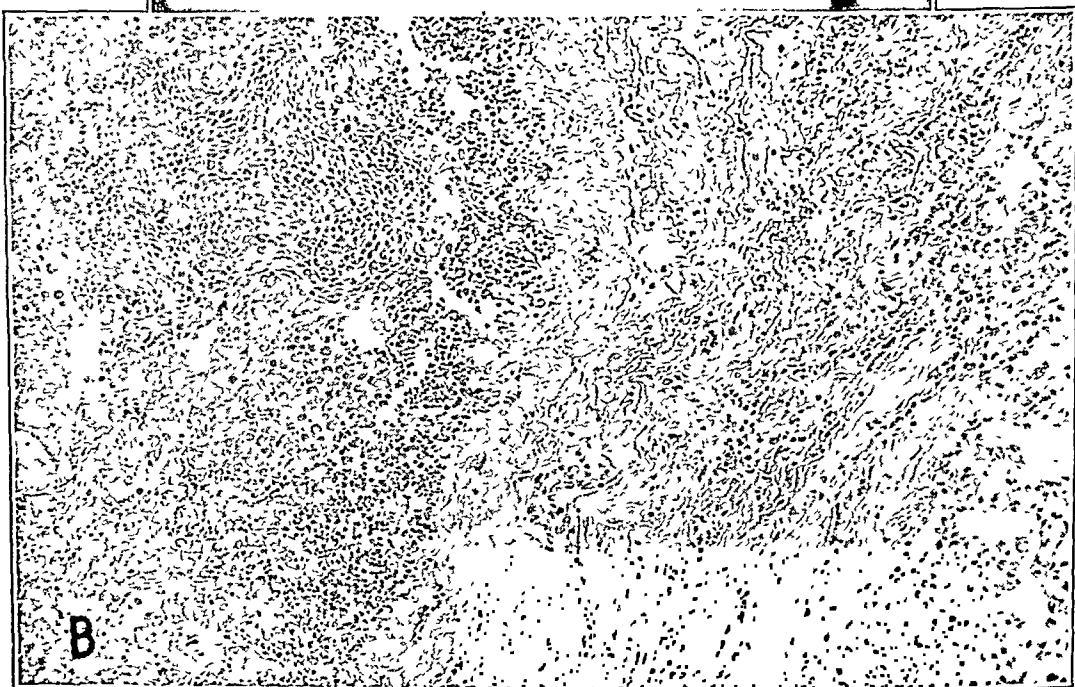
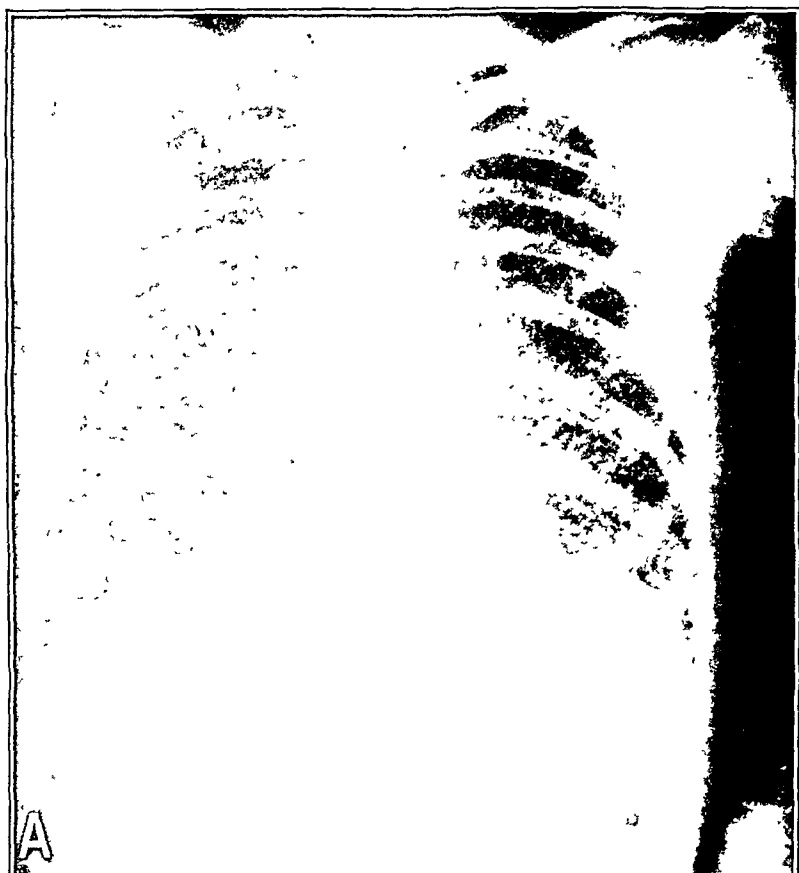


Fig. 7 (case 6).—*A*, roentgenogram of patient with metastatic malignant melanoma. *B*, photomicrograph showing good repair at site of biopsy.

adenocarcinoma was discovered in the pulmonary tissue (fig. 5B), a careful examination of the patient revealed the presence of a very small tumor in the right breast, later proved to be an adenocarcinoma.

CASE 5.—E. G., a 41 year old white housewife, complained of a chronic cough which in the last year had become associated with fatigue, shortness of breath and a low grade fever. There was no improvement in her condition after a period of rest in bed. Roentgen examination (fig. 6A) showed diffuse miliary infiltration in both lungs. The patient's husband had been exposed to beryllium, and for this



Fig. 8 (case 6).—Gross appearance at autopsy of lobe at site of biopsy.

reason a diagnosis of beryllium pneumonitis had tentatively been made. Sputum examination and blood studies were noncontributory. Pulmonary biopsy established a diagnosis of Boeck's sarcoid (fig. 6B). There has been pronounced clearing of the lesion without specific therapy.

CASE 6.—A. H., a 45 year old white farmer, was admitted to the hospital with known widespread metastatic melanoma from a primary lesion on the right arm, treated previously by radical resection. Roentgenograms (fig. 7A) showed multiple diffuse fine nodular tumor metastases throughout both pulmonary

fields. A pulmonary biopsy was performed to observe the effect of an experimental drug on the malignant cells. The biopsy confirmed the preoperative diagnosis of melanoma metastatic to the lung. The patient tolerated the biopsy well but died of debility one week later. At autopsy it was observed that there was excellent healing of the pulmonary tissue at the site of the biopsy with minimal pleural reaction (fig. 8). Microscopic sections through the area of biopsy revealed excellent repair (fig. 7B).

#### COMMENT

Biopsy of diffuse pulmonary lesions has now been used in a series of 50 patients. The procedure was well tolerated by the patients and produced little discomfort. No complications occurred which could be ascribed to the procedure. There was no dissemination and no pleural or wound infection in patients with bacterial and fungous diseases. Neither pneumothorax nor hemothorax has occurred in our cases as proved by postoperative roentgen studies. Transient minimal subcutaneous emphysema developed in 2 patients with pneumoconiosis and compensatory pulmonary emphysema, which, however, did not require treatment. The biopsy site was examined at autopsy in 1 patient with extensive metastatic melanoma; it showed excellent repair (case 6).

Biopsy of diffuse pulmonary lesions has permitted a rapid, accurate diagnosis of such conditions as tuberculosis, histoplasmosis, pneumoconiosis and sarcoidosis, as well as primary and metastatic carcinoma of the lung when the conventional present day methods available failed to establish the true nature of the disease process.

#### SUMMARY

A method of biopsy of diffuse pulmonary lesions is described. An accurate diagnosis of the pulmonary lesion was made in a series of 50 patients by the pathologic, bacteriologic or chemical examination of the biopsy specimen. The surgical procedure as described was well tolerated by the patient, producing minimal morbidity and no mortality.

# USE OF POLYETHYLENE IN EXTRAPLEURAL PNEUMONOLYSIS

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AND

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THE OPERATION of extrapleural pneumonolysis for tuberculosis was apparently first performed by Tuffier in 1891.<sup>1</sup> In its various modifications this operation has enjoyed several periods of popularity, only to suffer ensuing periods of disrepute. In the armamentarium of conservative thoracic surgeons it has come to occupy a definite, though minor, place in their treatment of pulmonary tuberculosis. For the most part, its use should be confined to cases in which thoracoplasty cannot or should not be done. Literally scores of various and different substances have been used to fill the artificially created, unnatural extrapleural space. The recent introduction of comparatively nonirritating plastic compounds, particularly lucite (an acrylic resin, methyl methacrylate) in the form of spheres, has again brought this operation into focus.<sup>2</sup> However, the use of lucite spheres has been condemned by Trent,<sup>3</sup> Murphy<sup>4</sup> and others. The relative hardness of the spheres has caused them to erode into lung,<sup>3</sup> ribs<sup>5</sup> and esophagus, and because of their size and shape they have at times drifted into other anatomic localities.

In July 1947, Grindlay and his associates<sup>6</sup> first reported their experimental and clinical studies on polyethylene film. Their experience gave use the idea that this film might be a more suitable substance for filling the extrapleural space than those in current use. This supposition has since proved to be true.

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Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 19, 1949.

1. Alexander, J.: *The Collapse Therapy of Pulmonary Tuberculosis*, Springfield, Ill., Charles C Thomas, Publisher, 1937.

2. Wilson, D. H.: *Extrapleural Pneumonolysis with Lucite Plombage*, J. Thoracic Surg. **17**:111-122 (Feb.) 1948.

3. Trent, J. C.; Moody, J. D., and Hiatt, J. S., Jr.: *An Evaluation of Extrapleural Pneumonolysis with Lucite Plombage*, J. Thoracic Surg., to be published.

4. Murphy, J. D., in discussion on Trent, Moody and Hiatt.<sup>3</sup>

5. Brown, R. K.: Personal communication to the authors.

6. Grindlay, J. H.; Brown, M. H., and Craig, W. McK.: *Preliminary Report on Experimental and Clinical Studies with Polythene Film*, Proc. Staff Meet., Mayo Clin. **22**:453-456 (July 17) 1947.



Polyethylene,<sup>7</sup> essentially a pure chemical compound,<sup>8</sup> a polymer of ethylene, is produced in the form of tough, flexible, elastic films of varying thicknesses. It is unwettable, light in weight (specific gravity 0.92) and transparent to roentgen rays and has a softening point above the temperature of boiling water.<sup>6</sup> Unlike many other plastic compounds, polyethylene holds sutures very well and has little tendency to tear. Grindlay found neither an inflammatory nor a foreign body reaction when polyethylene was buried in body cavities or tissues. Capillary-sized tubing inserted into veins has been left in place for as long as two weeks without plugging of the tube or reaction in the wall of the vein.<sup>9</sup> Thin films of polyethylene have been wrapped around severed tendons after suture and have very successfully prevented contiguous adhesions to surrounding structures.<sup>10</sup> We have implanted the film in the extrapleural space of dogs. Except for the initial effect of trauma produced by the operative procedure, no inflammatory reaction has been noted. The film lay as a completely inert material for as long as it was left in place. A great deal of confusion exists at present about tissue reaction produced by various types of polyethylene, and we do not wish to add more. Suffice it to say that the polyethylene film with which we have worked was apparently free from irritant plasticizers or other substances such as dicetyl phosphate which may have been used in the manufacture of this film for commercial purposes.<sup>11</sup>

Our clinical experience with polyethylene consists of its use in 21 cases of pulmonary tuberculosis for which extrapleural pneumonolysis was done. In the performance of this operation the posterior approach is used most frequently because we feel that better exposure is obtained than by the axillary or anterior route. A sufficiently long straight paravertebral incision is made to allow enough mobilization of the scapula so that a 3 or 4 inch (7.5 or 10 cm.) segment of either the third or the fourth rib may be removed. The cleavage plane separating the parietal pleura from the chest wall in the endothoracic fascia is

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7. Supplied by the Visking Corporation, Terre Haute, Ind.

8. Cahn, E. B.: Personal communication to the authors.

9. Guenther, T. A.; Grindlay, J. H., and Lundy, J. S.: New Flexible Capillary Tubing for Use in Venoclysis, *Proc. Staff Meet., Mayo Clin.* **22**:206-207 (May) 1947.

10. Gonzales, R. I.: Experimental Tendon Repair Within the Flexor Tunnels: Use of Polyethylene Tubes for Improvement in Functional Results in the Dog, *J. Bone & Joint Surg.*, to be published.

11. LeVeon, H. H., and Barberio, J. R.: Tissue Reaction to Plastics Used in Surgery with Special Reference to Telfon, *Ann. Surg.* **129**:74-83 (Jan.) 1949. Southworth, J. L.: Experimental Pulmonary Collapse, *ibid.* **129**:85-89 (Jan.) 1949. Yeager, G. H., and Cowley, R. A.: Studies on the Use of Polythene as a Fibrous Tissue Stimulant, *ibid.* **128**:509 (Sept.) 1948.

developed under direct vision. The size and contour of this artificially created space is determined by the localization and extent of the lesion. Usually the extent of the tuberculous process makes mandatory complete mobilization of the apex of the lung and separation of the parietal pleura from the mediastinal structures inferiorly to the aortic arch or the azygos vein. Once this space has been created, polyethylene film is inserted for its permanent maintenance. Initially a single large pack of fluffed-up film was roughly molded by hand into the general desired shape and inserted. We have found, however, that this type of pack shrinks somewhat in size in the following months (fig. 1). At present we are lining the cavity with a single thin sheet and then putting in long strips of the film to form a firm but resilient pack. This type of pack has not decreased in size as much as the former one (fig. 2).



Fig. 1.—Decrease in size of an extrapleural polyethylene pack over a period of six months in a patient aged 62.

We have been rather conservative in our indications for the use of this procedure and have limited it largely to patients in whom thoracoplasty was not advisable—i. e., aged persons (our oldest patient was 65 years old), patients with preexisting contralateral thoracoplasty and persons whose pulmonary function precluded the less specific collapse afforded by thoracoplasty. There have been no deaths in this series of patients and no severe operative complications. Since our first use of this material, in December 1947, no patient has had a clinical infection of the extrapleural space. So far as can be determined, no erosion of an adjacent structure has taken place, and there has been no shifting in the location of the pack. The fact that closure of the cavity has not always taken place is due not to the substance used but to the inefficiency of the operation itself and the nature of the underlying disease.

Our clinical use of polyethylene film has shown it to have several distinct advantages. The film may be so used that it will completely fill the varying irregularities of the space. The pack may be made of any degree of hardness. It is easily sterilized, is easily handled in the operating room and requires no unusual instruments. Definitely advantageous is the fact that the material may be sutured to maintain its correct position. This characteristic was fortunately demonstrated when the free pleural space of 1 patient was inadvertently entered inferiorly at the completion of the stripping of the parietal pleura from the chest wall. The impossibility of closing this tear satisfactorily precluded the use of lucite spheres or paraffin. However, we were able to insert a polyethylene pack and suture it to the adjacent intercostal bundles. We have followed this patient's progress in the ten months since operation, and the pack has remained in its original position.

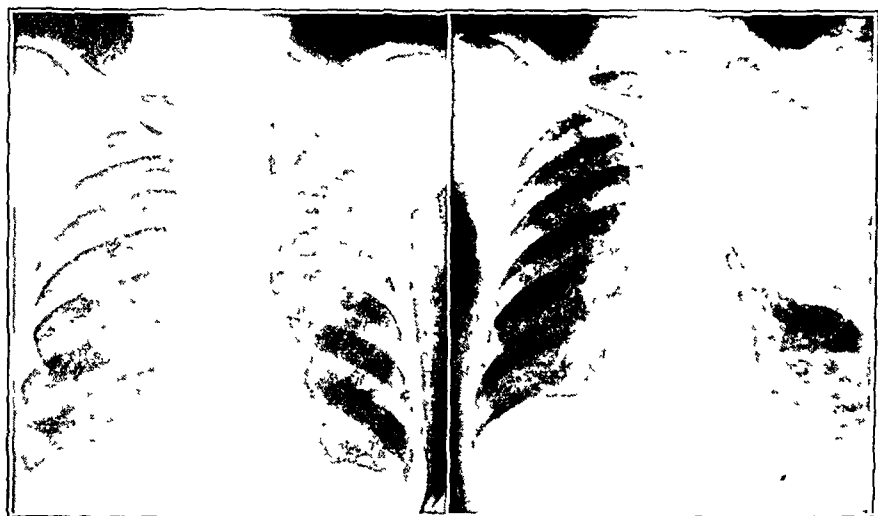


Fig. 2.—Large extrapleural polyethylene pack which did not decrease in size in a period of nine months (patient aged 65).

Such a pack may also be removed without difficulty. In 1 of our patients, closure of the cavity was not obtained, and nine months after the initial extrapleural pneumonolysis the pack was taken out easily and thoracoplasty performed because the patient's condition had improved sufficiently to permit that procedure. At the time of this operation the extrapleural space contained no free fluid and was not lined with a fibrous sac. In fact, after the pack had been in place for nine months, the cavity looked as though it had just been created and showed no gross visible reaction of any type. With positive pressure, the exposed lung covered by both visceral and parietal pleuras expanded fairly well. However, for academic reasons, a section of pleura was removed from the underlying lung; it proved to be a

layer of well organized fibrous tissue approximately 0.8 mm. thick. The pack itself was unchanged and had not deteriorated. When the various sheets of this pack were unfolded, they looked just as they had originally (fig. 3).

Our experience has shown that the disadvantages of this entire procedure have been those which are primarily inherent in the operation itself. Moreover, the fact that a polyethylene pack may decrease in size in the months after its insertion may or may not be a disadvantage.

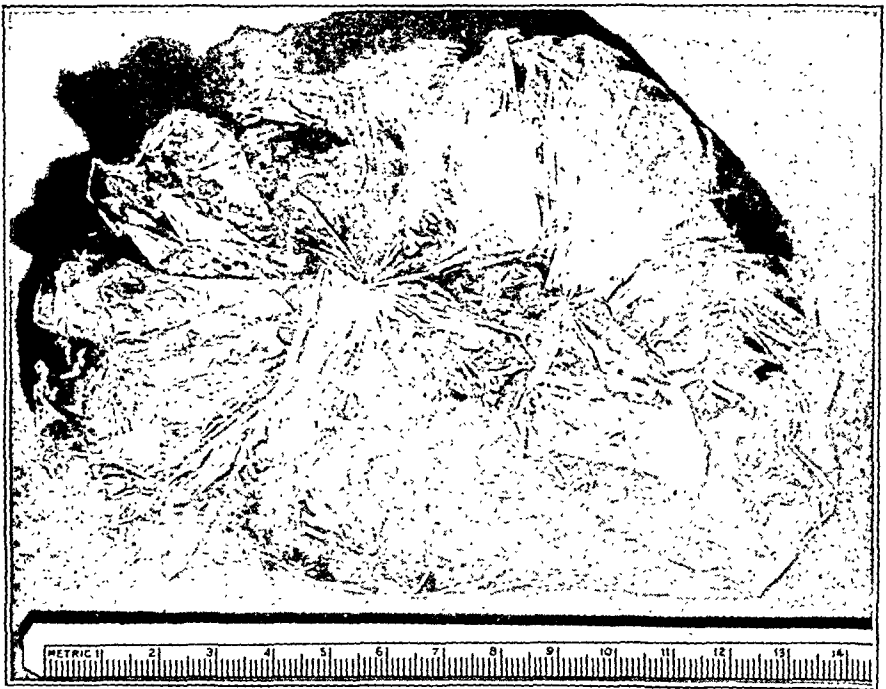


Fig. 3.—Polyethylene pack removed from extrapleural space after nine months.

#### SUMMARY

Polyethylene film has been used as a filling in extrapleural pneumonolysis in 21 patients. It has fulfilled certain essential requirements and has so far been the best substance for this use that we have encountered. No attempt has been made in this presentation to evaluate the operation itself in its relation to pulmonary tuberculosis. However, we wish to emphasize our belief that it occupies a definite, though minor, place in our treatment of the disease.

## "SPONTANEOUS" RUPTURE OF THE ESOPHAGUS

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In the byeways of surgery there can be few conditions more dramatic in their presentation and more terrible in their symptoms than spontaneous perforation of the oesophagus. No case has yet been treated successfully, and diagnosis has only been achieved in a very few before death, and yet there is no fundamental reason why this unsatisfactory position should not be improved in the future. Several things are essential to success: firstly, a knowledge that the accident can and does occur; secondly, a knowledge of the symptomatology; and, thirdly, an early diagnosis. Given these, I am convinced that surgeons will be able to save some of these patients by combining the principles, already well established in the cases of abdominal perforations, with those relevant to thoracotomy.—N. R. Barrett.<sup>1</sup>

WITH the preceding words, Barrett, in 1946, reported the fact that of 50 patients with spontaneous rupture of the esophagus whose cases were recorded in the world literature from 1724 to that date not one had survived. Several cases of survival have been reported in the past year; in the majority of them the condition was diagnosed only after rupture into the pleural cavity, and the subsequent course was a long and stormy convalescence.

It seemed, therefore, of value to report a case in which so-called spontaneous rupture of the esophagus occurred, the condition being detected and operated on before perforation of the pleura ensued, the end result being a rapid cure.

### REPORT OF A CASE

A. D., a veteran, 30 years of age, while playing hockey sustained several very severe knocks, one in particular "knocking his wind out" completely. He paid no particular attention to this, however, and experienced no symptoms until the next morning. During breakfast he noticed a sudden, severe, burning pain in the pit of his stomach; in particular one piece of toast seemed to irritate something deep in his chest and he vomited. He went to work, but by 11 o'clock the burning pain was so severe that he could no longer stand. The burning finally became so severe that he requested admission to a hospital. On arrival, he stated that for about two years he had noticed the sensation when eating "as though food were

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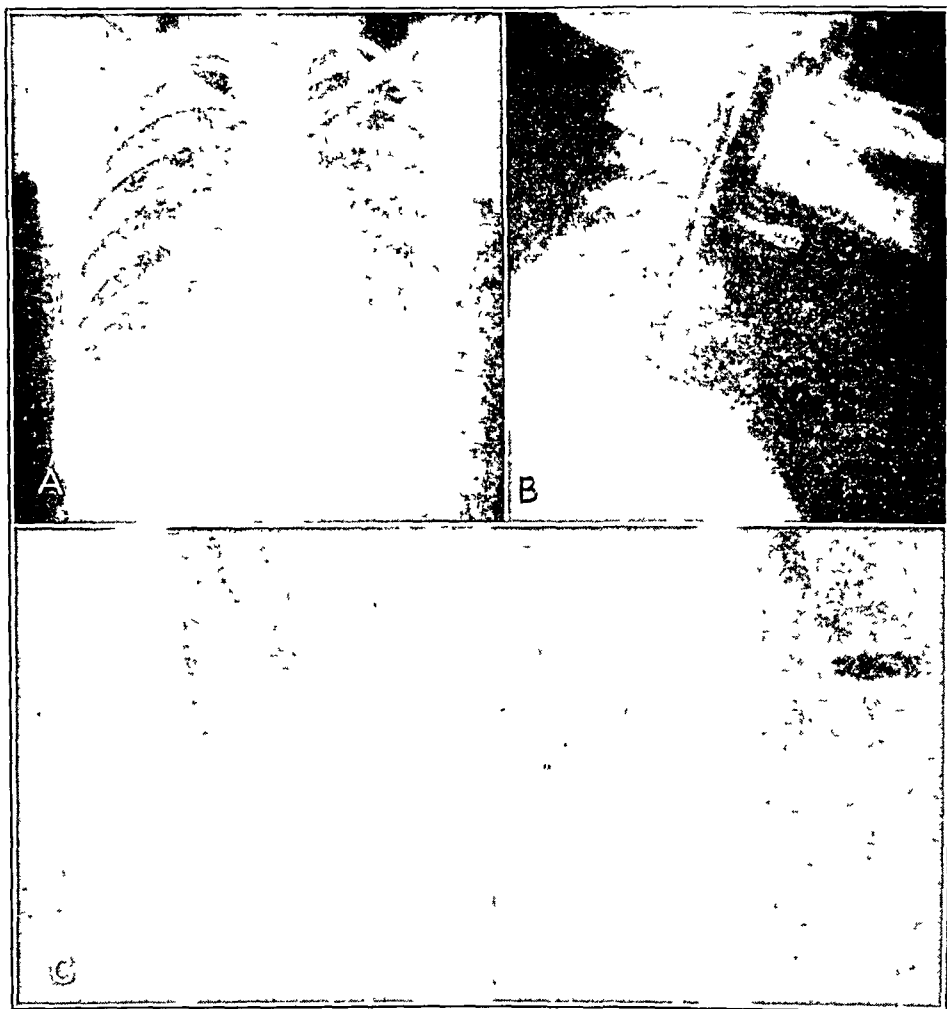
From the Queen Mary Veterans' Hospital.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 19, 1949.

1. Barrett, N. R.: Spontaneous Perforation of the Oesophagus: Review of the Literature and Report of Three New Cases, *Brit. Surg.* 1:48 (March) 1946.

going down the wrong way." When this occurred he would leave the table and retch voluntarily. This seemed to clear this abnormal sensation, and he could then continue with his full and regular meal. There was no history of intolerance to any food or any other disease related to his gastrointestinal tract.

Examination on admission revealed a temperature of 99 F., a pulse rate of 88 and a respiration rate of 34. In addition to the rapid rate, the breathing was shallow and irregular. Examination of the chest revealed a few rales at the base of the left lung and short, shallow, rapid, irregular respiration of catching



*A*, apparently normal roentgenogram of the chest following perforation (this is one of the greatest causes of mistakes in diagnosis); *B*, lateral view of the neck showing column of air between the esophagus and vertebra; *C*, barium swallow showing escape of barium between the eighth and ninth vertebra.

type Otherwise the chest and the cardiovascular system were normal. The blood pressure was 116 systolic and 56 diastolic. On examination of the neck crepitus could be felt

The abdomen was tense and firm. The whole abdominal wall showed "guarding," more particularly in the upper quadrants. With persuasion this resistance

could be broken through. Tenderness was generalized, again more so in the upper half. No masses were palpable. No tenderness was detected in the lumbocostal region. (The abdominal condition was typical of that seen following perforation of a peptic ulcer.) Because of the rapid respiration rate, a roentgenogram of the chest was taken.

Within a few hours of admission the temperature reached 102 F.

In view of the rapid respiration, crepitus in the neck and rigidity of the abdomen a tentative diagnosis of rupture of the esophagus was made and a barium sulfate swallow was given. A curious conformation of the barium opposite the eighth thoracic vertebra confirmed the impression.

After establishment of the diagnosis a posterior mediastinotomy was done by the removal of the vertebral ends of the eighth and ninth ribs on the right side. The pleura was easily stripped away from the posterior thoracic wall and was intact, but as the esophagus was reached, the pleura was torn slightly and a small amount of clear, thin fluid drained from the right thoracic cavity. The esophagus was at first mistaken for the aorta because, instead of being soft and pliable, it was hard and indurated, actually resembling a length of rubber hose. The finger was slipped along the esophagus almost to the dome of the pleura, and only at this point did the esophagus begin to assume its normal consistency. As the finger was passed up, a considerable amount of thin purulent fluid came down from above. On closer examination at the level of the eighth thoracic vertebra, a small amount of pus was seen exuding from a tiny hole on the anterior surface of the esophagus. The outer coats of the organ at this point were opened and about a teaspoon of yellow pus, which seemed to have been contained within the muscular wall, was evacuated. A small hole into the mucosa was then found by a probe. It was impossible to determine the extent of this hole without doing serious damage to the esophageal wall. A Levin tube was then passed into the stomach from the mouth and two drains were installed: one, a Levin tube to the actual site of perforation, and the other, a sheath rubber drain to the hole in the pleural cavity. The latter was then packed off with gauze.

After operation the right lung was found to be collapsed and air was aspirated three times; thereafter full expansion occurred.

The packing and sheath rubber drain were removed in six days, the other drainage tube being left in place. One week following operation, the patient was allowed to drink and was also given methylene blue each day. The dye appeared on the thoracic dressing for five more days and then ceased. The Levin tube was removed from the stomach on the fifteenth day and the mediastinal drainage tube at the same time. All symptoms had disappeared in eighteen days, and on the twenty-first day the patient was on an unrestricted diet and was allowed to go home. On the twenty-sixth day he returned for examination and a small collection of pus was found in the wound, which was reopened slightly. However, dye given by mouth did not appear on the dressing, and a roentgenogram of his chest showed no abnormalities. All symptoms completely disappeared within forty-eight hours, and he has remained normal ever since. The usual antibiotic therapy was continued throughout his treatment.

Shortly before this patient was observed, the autopsy findings of a case of spontaneous perforation of the esophagus were shown in the hospital, and I had read Barrett's article, which emphasized the ease of diagnosis of this condition if the triad of symptoms is remembered.

The cause of this condition is unknown; hence the rather poor term "spontaneous." Apparently the precipitating factor is a sudden increase in intraesophageal pressure, brought on by forceful vomiting, straining or external trauma to the abdomen or thorax. In practically all cases coming to autopsy there is a tear in the esophagus, with mediastinitis and pleuritis. On microscopic examination of the tissues around this tear, lesions have not been found. One must conclude, therefore, that at the moment all theories as to the cause are purely speculative and the treatment is therefore empiric.

#### SUMMARY

A case of spontaneous rupture of the esophagus with cure is reported.

The triad of symptoms—rapid respirations, rigidity of the abdomen and crepitus in the neck—is emphasized.

The urgency of mediastinotomy is stressed.

No cause for the condition is known.



## INTRAVENOUS ADMINISTRATION OF PROCAINE HYDROCHLORIDE DURING GENERAL ANESTHESIA

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AND

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DETROIT

THE RELATIVELY recent discovery of the fact that procaine can be administered intravenously to people without serious results and even with benefit in some circumstances, has stimulated renewed interest in the pharmacology of this drug. It has been taught for some years that inadvertent intravenous injection of procaine hydrochloride was very dangerous because of its tendency to produce serious systemic reactions in the form of either circulatory depression or generalized convulsions. While these teachings were not entirely erroneous, they must be revised to take into account the rate and concentration of injection.

Experiments carried out by Eggleston and Hatcher,<sup>1</sup> published in 1916 and 1919, furnished a background for the possibility of the intravenous administration of procaine. They reported that cocaine and holocaine® were destroyed rather slowly when administered intravenously but that procaine and several other drugs used for local anesthesia were rapidly destroyed when administered intravenously to animals. They were able to repeat a sublethal dose every twenty minutes in these animals without evidence of accumulation. Also, they were able to give the drug continuously, with the result that large amounts were well tolerated over a period of time. The drugs they studied produced similar symptoms when rapidly administered to animals in one sublethal dose. They reported that they usually found a fall in blood pressure, respiratory arrest, slowing of the pulse rate and a few generalized convulsions, and then the animal rapidly returned to normal. A known fatal dose caused prompt cessation of the heart and respira-

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Read at the Sixth Annual Meeting of the Central Surgical Association, Feb. 19, 1949.

1. Hatcher, R. A., and Eggleston, C.: A Contribution to the Pharmacology of Novocaine, *J. Pharmacol. & Exper. Therap.* 8:385-405 (May) 1916. Eggleston, C., and Hatcher, R. A.: A Further Contribution to the Pharmacology of the Local Anesthetics, *ibid.* 13:433-487 (June) 1919.

tion usually combined with generalized extensor spasm. They believed that the drop in blood pressure was due to the action of the drug on the heart and not to vasodilatation. From in vitro experiments they concluded that the drug was destroyed by the liver. For measures of resuscitation they advised artificial respiration, with or without cardiac massage, and intravenous injection of epinephrine in cases of severe circulatory depression. These workers did not suggest any likely therapeutic value from intravenous use of procaine. They stated that the literature abounded with reports of severe toxic symptoms from the clinical administration of procaine and other drugs during the course of local anesthesia. Therefore, it is not to be wondered that the intravenous administration of these drugs was studiously avoided.

During the last ten years there has been an ever increasing use of procaine hydrochloride by the intravenous route. Lewy<sup>2</sup> reported administering procaine intravenously to treat tinnitus aurium; Lundy<sup>3</sup> used it by this route to treat pruritus, and Burstein<sup>4</sup> used it to depress cardiac irritability. The use of dilute concentrations, given over a period of time, for therapeutic purposes was reported by Graubard and Peterson.<sup>5</sup> Gordon<sup>6</sup> used procaine intravenously to relieve the pain for débridement of burns. McLachlin<sup>7</sup> used procaine by this route in relieving postoperative pain. Allen<sup>8</sup> was one of the first to use large amounts intravenously in an effort to produce analgesia for childbirth. He administered 1 to 2.5 Gm. per hour in a continuous intravenous drip and treated any convulsions that occurred with intravenous injection.

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2. Lewy, R. B.: Treatment of Tinnitus Aurium by the Intravenous Use of Local Anesthetic Agents, *Arch. Otolaryng.* **25**:178-183 (Feb.) 1937.

3. Lundy, J. S.: *Clinical Anesthesia*, Philadelphia, W. B. Saunders Company, 1942, p. 392.

4. Burstein, C. L., and Marangoni, B. A.: Protecting Action of Procaine Against Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia, *Proc. Soc. Exper. Biol. & Med.* **43**:210-212 (Jan.) 1940. Burstein, C. L.; Marangoni, B. A.; DeGraff, A. C., and Rovenstine, E. A.: Laboratory Studies on the Prophylaxis and Treatment of Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia, *Anesthesiology* **1**:167-186 (Sept.) 1940. Burstein, C. L.: Treatment of Acute Arrhythmias During Anesthesia by Intravenous Procaine, *ibid.* **7**:113-121 (March) 1946.

5. Graubard, D. J.; Robertazzi, R. W., and Peterson, M. C.: Intravenous Procaine: A Preliminary Report, *New York State J. Med.* **47**:2187-2192 (Oct.) 1947; Microdeterminations of Blood Levels of Procaine Hydrochloride after Intravenous Injection, *Anesthesiology* **8**:236-240 (May) 1947.

6. Gordon, R. A.: Intravenous Novocaine for Analgesia in Burns, *Canad. M. A. J.* **49**:479-481 (Dec.) 1943.

7. McLachlin, J. A.: The Intravenous Use of Novocaine as a Substitute for Morphine in Postoperative Care, *Canad. M. A. J.* **52**:383-386 (April) 1945.

8. Allen, F. M.: Intravenous Obstetrical Anesthesia, *Am. J. Surg.* **70**:283-290 (Dec.) 1945.

tions of pentothal sodium.<sup>9</sup> Fraser<sup>9</sup> reported 400 intravenous administrations of procaine hydrochloride in 0.1 to 0.2 per cent solution in combination with pentothal sodium<sup>9</sup> during anesthesia. Barbour<sup>10</sup> reported on its use as a therapeutic drug, and Brodie, Leif and Poet<sup>11</sup> reported on the fate of intravenously administered procaine in man. Our interest in this therapy was stimulated by the report of Bittrich and Powers,<sup>12</sup> who used 1 per cent procaine hydrochloride solution intravenously during anesthesia and operation. They reported that it produced a depression of the cough reflex, decreased cardiac irritability and resulted in an inhibition of sweating. Although we have administered procaine in this way to approximately 400 patients, only a few more than 200 of the cases have been carefully analyzed. The only phase of this topic that will be discussed is the intravenous administration of procaine hydrochloride continuously during general anesthesia as an adjunct and not as the primary anesthetic drug.

Although this method can be used with almost any type of general anesthesia, our use of the drug has been limited to about three combinations. The first, and most frequently used method, consists in induction with pentothal sodium,<sup>9</sup> with or without curare, usually followed by endotracheal intubation and a continuous flow of nitrous oxide and oxygen plus intravenous administration of procaine hydrochloride throughout the anesthesia. This combination is frequently used in thoracic surgery, either for procedure on the thoracic cage or for trans-thoracic work. Another combination is the use of cyclopropane combined with administration of procaine intravenously. In still fewer instances, we have administered procaine intravenously in combination with ether anesthesia. It may be less important with ether, a drug which is efficient in depressing troublesome reflexes itself. However, one may maintain much lighter ether anesthesia and prevent excessive saturation of the tissues during a prolonged anesthesia.

The technic consists in making 500 or 1,000 cc. of 1 per cent procaine hydrochloride in 5 per cent dextrose solution by dissolving 1 Gm. of sterile procaine hydrochloride crystals to each 100 cc. of the infusion fluid to be used. This must be well shaken to insure complete dissolving of the crystals. This is administered through a needle separate from all other fluids, in order that its rate can be

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9. Fraser, R. J.: Intravenous Pentothal Procaine Analgesia, *Anesth. & Analg.* **27**:159-163 (May) and 282-285 (Sept.) 1948.

10. Barbour, C. M., and Tovell, R. M.: Experience with Procaine Administered Intravenously, *Anesthesiology* **9**:514-523 (Sept.) 1948.

11. Brodie, B. B.; Leif, P. A., and Poet, R.: The Fate of Procaine in Man Following its Intravenous Administration and Methods for the Estimation of Procaine and Diethylaminoethanol, *J. Pharmacol. & Exper. Therap.* **94**:359-366 (Dec.) 1948.

12. Bittrich, N. M., and Powers, W. F.: Intravenous Procaine in Thoracic Surgery, *Anesth. & Analg.* **27**:181-196 (July) 1948.

carefully controlled. The rate is determined by counting the number of drops per minute, made possible by an ordinary dropper in the intravenous tubing. Administration of procaine is usually started shortly after surgical anesthesia has been produced by the principal drug, and the flow is started at a rate of 30 to 60 drops per minute, which amounts to about 2 to 4 cc. per minute or 20 to 40 mg. of procaine hydrochloride per minute. When pentothal sodium® is used for induction, there is no need for rapid rates of flow early in the anesthesia in most circumstances but it may be necessary to increase the rate as the effect of the pentothal sodium® decreases. The blood pressure must be watched carefully, and severe drops of pressure, regardless of the cause, indicate necessity to decrease or stop the flow of procaine until the cause of the drop in blood pressure has been determined and corrected. An average rate of 2 to 4 Gm. an hour is usually sufficient.

Clinical observation has revealed the following desirable effects from procaine during various types of anesthesia:

1. The cough reflex is depressed even when an endotracheal airway is in place or there is manipulation within the pleural cavity. This is not an absolute obtundation of the cough reflex, but it is a strong tendency to depress this reflex without otherwise deep anesthesia. Many times severe "bucking" has been controlled by procaine alone without interference with the patient's breathing.

2. It has been effective in preventing cardiac arrhythmias during most intrathoracic operations with cyclopropane. Again, this is not absolute but is a marked depressing effect on the cardiac irritability.

3. Sweating is inhibited; the skin remains warm and dry; occasionally the hands will be cool and dry. For the most part, this is a desirable action; however, it is possible that during hot weather depression of sweating will not be desirable.

4. The entire respiratory tract is usually very dry, and excessive salivation, nausea, retching and vomiting during recovery are very rare. The patients can retain fluids by mouth as soon as desired after recovery.

5. Intravenous administration of procaine is helpful in maintaining light anesthesia with any anesthetic drug, probably because of the drying of secretions, controlling of the cough reflex and producing of some analgesia. Many trials have demonstrated that it plays a part in maintaining anesthesia with light levels of surgical anesthesia.

6. It results in postoperative analgesia from twenty minutes to several hours, thus accounting in large measure for the recovery to consciousness without excitement. This has been particularly noticeable in patients recovering from cyclopropane.

7. The results in some types of operations are striking enough to be appreciated by both the anesthesiologist and the surgeon. The patients have been well pleased.

The disadvantages and dangers of intravenous administration of procaine hydrochloride are the following:

1. It increases the technical aspect of anesthesia by necessitating a separate infusion set and needle with careful control of the rate of flow. At the present time, we are able to get procaine crystals in 5 Gm. vials, and it is hoped that in the future procaine in solution may be available to avoid the necessity of dissolving crystals.

2. The greatest danger in the intravenous use of procaine is the possibility of circulatory depression, which may occur rather rapidly in case of an overdose. If pentothal sodium<sup>®</sup> is being used, this may occur without any convulsive manifestations being present. If cyclopropane is being used, this drop in blood pressure is rarely seen because convulsive manifestations usually occur before the circulatory depression. It is best to limit the rate of flow to 4 to 5 cc. per minute for an average adult and less for the elder patients.

3. The possibility of convulsive phenomena is always present; however, since we watch the patient constantly, we have no great fear of this complication because it can be controlled either by intravenous administration of a barbiturate or by decreasing the rate of flow of procaine. It is practically always preceded by facial twitching. Only once in 200 cases was pentothal sodium<sup>®</sup> given to control a convulsion.

4. There may be other dangers involved which we have not yet encountered, such as damage to parenchymatous organs or other tissue cells. Frequently, it takes several hundred cases to discover rarely occurring damage of this sort. To date, we have not observed any, in spite of fairly large doses to some patients.

There are three general types of operation in which procaine has been found the most advantageous. The first is thoracic or trans-thoracic operations; we have found it beneficial in depressing the periorsteal and laryngeal reflexes, in depressing the cough reflex, in drying up secretions of the respiratory tract and also in providing postoperative analgesia. For intrathoracic operations it has been helpful in depressing cardiac irritability, but it has not been found that it is absolute in blocking vagovagal reflexes.

A second type of operation in which it has been found useful is in anesthesia for thyroidectomy. While the anesthesia for thyroidectomies does not present as serious problems as before the days of propylthiouracil, one can readily appreciate the stabilizing effect of intravenously administered procaine during this type of operation. The recovery has been smoother, and one is led to believe that a thyroid crisis might well be treated with intravenous procaine. The third group comprises operations of a superficial nature in which light anesthesia is adequate for the operative procedure. Such an operation can be performed either with

or without an endotracheal airway when procaine is administered. In these patients, smaller amounts of procaine are used.

Chart 1 is a copy of the anesthesia record during the intravenous use of procaine. It shows the patient's blood pressure and pulse during an intrathoracic operation. Induction was carried out with pentothal sodium,<sup>®</sup> cocaine was sprayed on the larynx, an oral endotracheal tube was inserted for the airway and the rest of the anesthesia was completed with nitrous oxide and procaine hydrochloride intravenously. The rate of flow of procaine is indicated in drops per minute. This patient received a total of 5 Gm. of procaine hydrochloride in one hour and

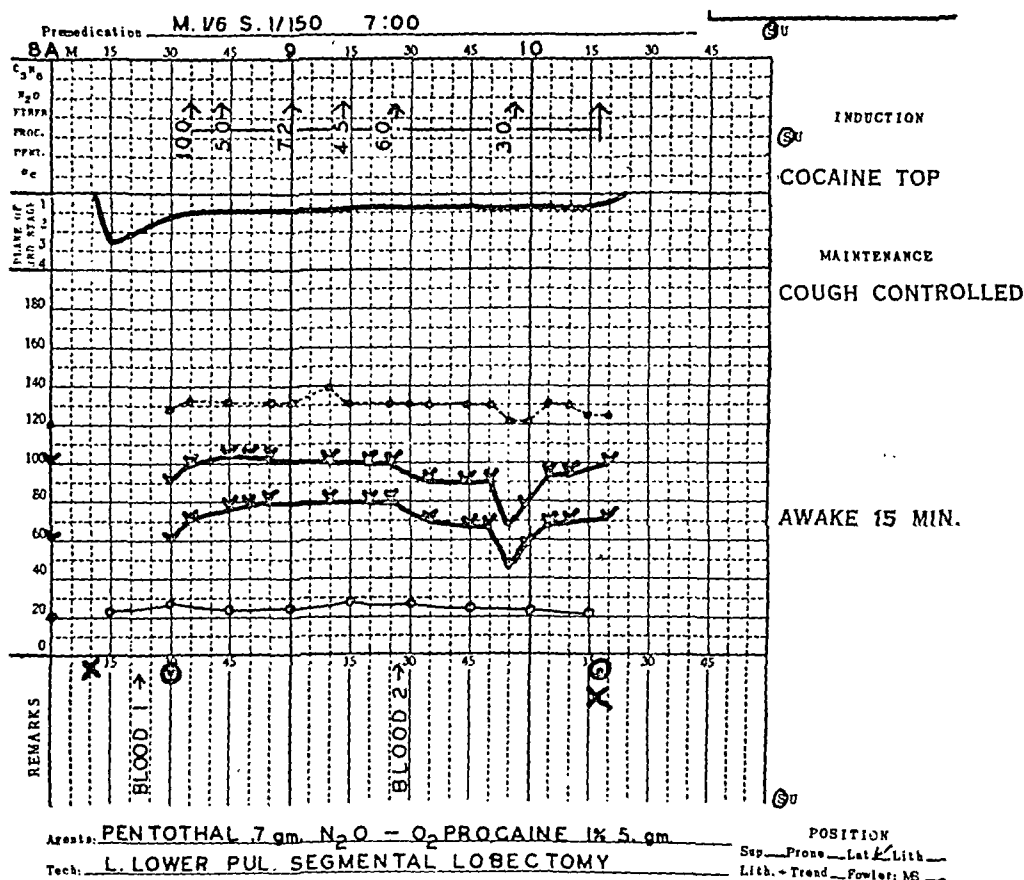


Chart 1.—Anesthesia record during an intrathoracic operation.

forty-five minutes. No pentothal sodium<sup>®</sup> was added after the induction, which was accomplished with 0.7 Gm. of the drug. Recovery to consciousness in this patient was slow, although reflexes were recovered immediately. The patient had twenty minutes' analgesia after return to consciousness.

Chart 2 is the record of anesthesia during thyroidectomy. The patient was a husky 30 year old man whose basal metabolic rate was no longer elevated after treatment with propylthiouracil. Induction of anesthesia was accomplished with pentothal sodium<sup>®</sup> mixed with d-tubocurarine and administered intravenously. The larynx was sprayed with 10 per cent cocaine solution before intubation. An oral endotracheal tube was inserted for an airway and used to replace the

mask. One point of interest in this case was a period of tachycardia that lasted some twenty minutes that was thought to be due perhaps to procaine, as the rate decreased after the rate of flow of procaine had been decreased. This patient received a total of 8 Gm. of procaine hydrochloride over a period of two hours and forty-five minutes. His recovery was immediate on discontinuation of the nitrous oxide and procaine; he had no vomiting and no pain and was not excited. It was not necessary to add any pentothal sodium® after the induction, even though there was an endotracheal tube in place and anesthesia with nitrous oxide was very light. The patient had no pain in his neck for thirty minutes after recovery to consciousness.

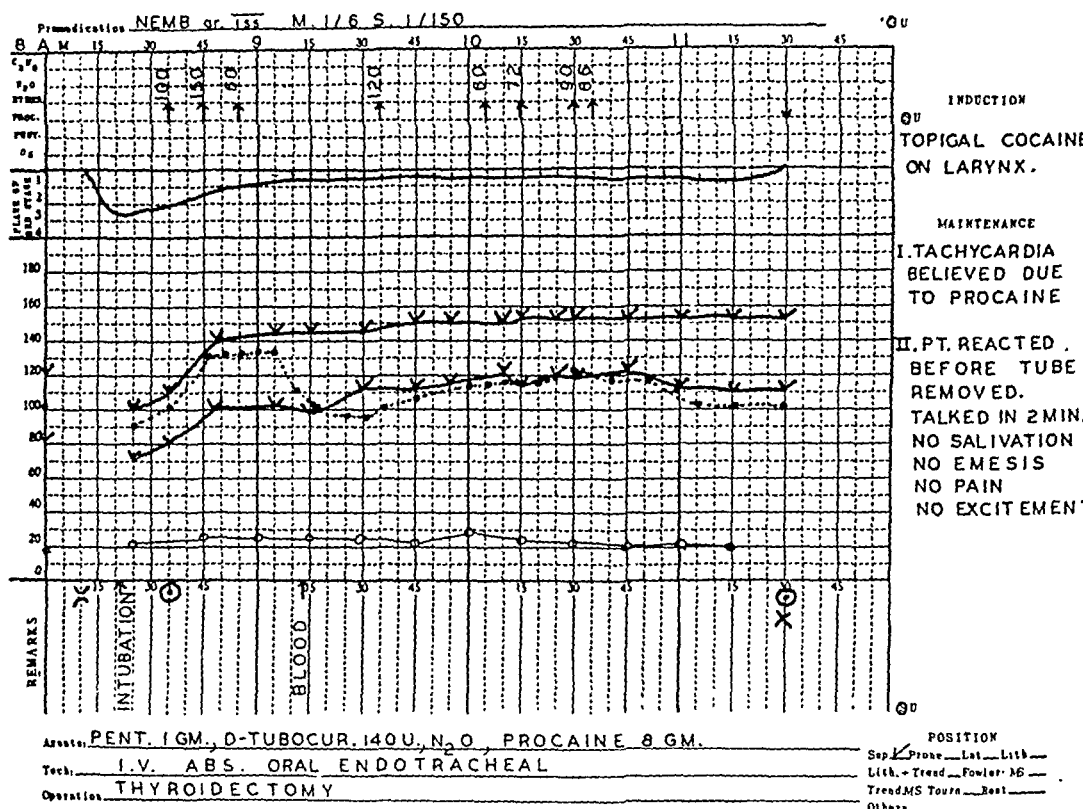


Chart 2.—Anesthesia record during a thyroidectomy.

Chart 3 is the record during anesthesia and operation on a 47 year old woman who had considerable hypertension before the anesthesia was started. The initial drop in blood pressure was produced by unconsciousness and the depressant effect of pentothal sodium® used for induction. The secondary depression of blood pressure was due to an overdose of procaine, as the blood pressure rose again after the rate of procaine was reduced. The second drop in blood pressure was intentionally produced by an overdose of procaine. The rate was increased to 120 drops, about 80 mg. per minute, and, after a period of ten minutes following a 20 mm. rise of systolic pressure, the blood pressure dropped. Softness of the pulse was noted, and the blood pressure was immediately taken; it was found that a drop of nearly 100 mm. of mercury had occurred. Use of procaine was immediately discontinued without changing anything else, and after a few minutes

the pressure again rose to its previous level. Except for weakness in pulse, reflecting the change in blood pressure, there were no other obvious changes in this patient during all this time. This a good demonstration of the rapidity with which circulatory depression can occur and the entire lack of warning signs except of the circulation itself. The drop in blood pressure is generally more gradual with ordinary rates of flow. One should not administer 1 per cent procaine hydrochloride faster than 6 cc. per minute and should then watch the circulation very closely.

Chart 4 presents the anesthesia record of a 74 year old man who was mentally confused before operation. He had auricular fibrillation, avitaminosis,

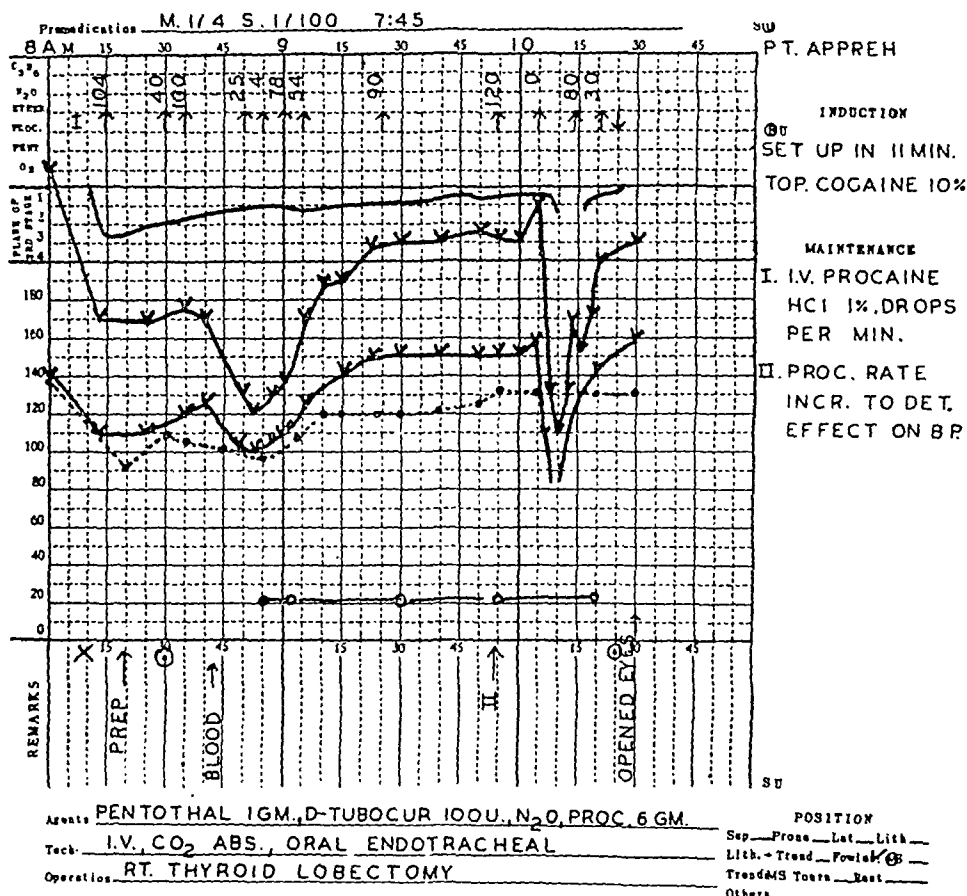


Chart 3.—Anesthesia record during an operation on a patient with hypertension.

generalized arteriosclerosis, chronic alcoholism and a fracture of the neck of the left femur. Anesthesia was induced with pentothal sodium® intravenously, followed by nitrous oxide and oxygen and procaine by the intravenous route. An overdose of procaine resulted in a marked drop in blood pressure and a complete disappearance of pulse. Respiratory arrest also occurred; the patient was definitely cyanotic. Vigorous inflation of the lungs with oxygen did not improve the patient's color. This obviously meant that the cardiac action was either stopped or insufficient. Epinephrine hydrochloride (1 mg.) was injected intravenously and forced in by intravenous solution. Thirty seconds later a palpable pulse was noted, and in two minutes the patient's color improved and in about five minutes the blood pres-



sure had returned to a fair level. After fifteen minutes, the respirations were resumed by the patient, although there was no light reflex of the pupils. The operation was not done. On the following day, the patient returned to his previous mental state; one week later, the operation was performed under open drop ether anesthesia. This represents the nearest to a fatality that has occurred in our series. The trouble was due to failure to observe the patient's circulation closely and also to the excessive dose of procaine to an elderly patient. It has been found that only about half the amount of procaine is necessary for elderly as for younger patients.

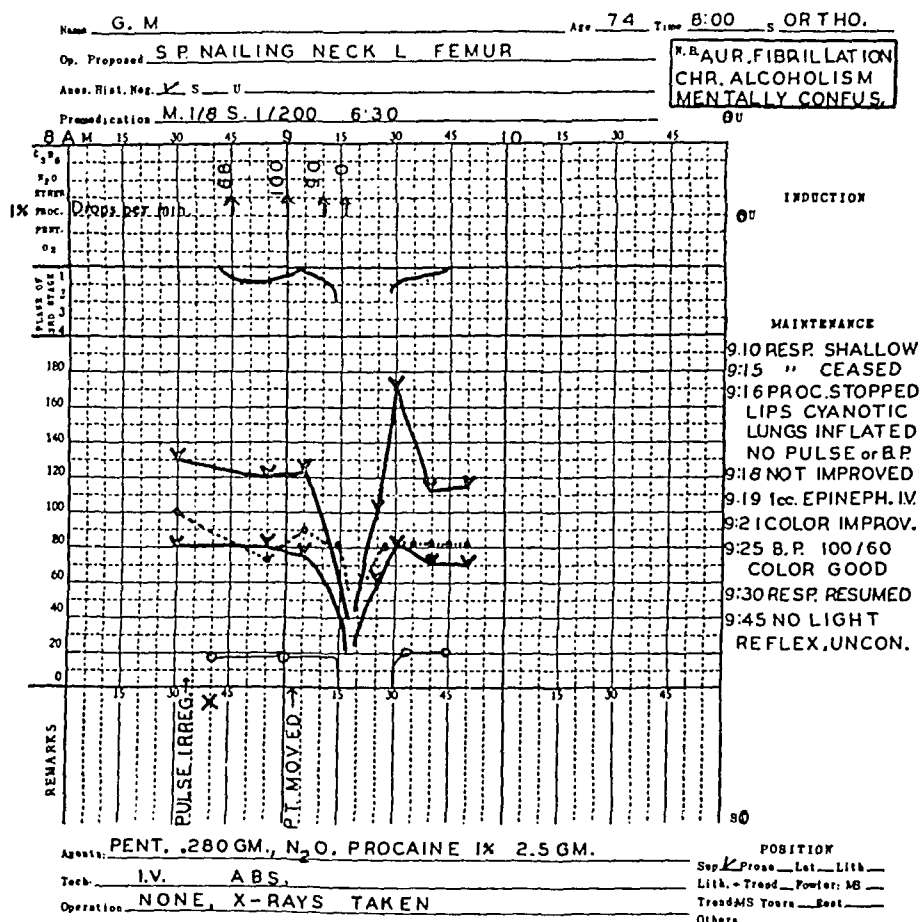


Chart 4.—Anesthesia record during an operation on a 74 year old man with avitaminosis, auricular fibrillation and generalized arteriosclerosis.

#### COMMENT

The use of 1 per cent procaine hydrochloride intravenously during general anesthesia has a definite value in certain type of anesthesia. The chief danger is circulatory depression caused by an overdose. This potential hazard may prove to be of sufficient magnitude to preclude the use of this drug in sufficient quantity to be of value. At the present time it appears that use of a sufficient quantity to assist in producing anesthesia places the method in the same category as the administration

of deep cyclopropane or chloroform anesthesia as far as the alertness necessary in watching the circulation is concerned. Lower and safer doses are of benefit in depressing some reflexes and are preferred in the light of the experience to date. Hence, 4 cc. per minute is the maximum for young adult patients, and not more than half that amount should be given to elderly patients. The effect it may have in preventing edema under casts or in the operative field has not been studied but has been suggested by Gordon.<sup>13</sup> For the most part, the use of procaine in this way represents a new purpose for a drug during anesthesia, and probably we are not too well prepared to measure its benefits. It has been appreciated for some time, however, that most drugs that produce general anesthesia are lacking in power to depress certain reflexes and functions, even though in most respects they are highly desirable. Ether is one drug that in higher concentrations depresses nearly all reflexes, and its over-all safety is recognized, but it is not pleasant for most patients and disturbs metabolism considerably. It is possible that better anesthesia will be possible with drugs like nitrous oxide and pentothal sodium<sup>®</sup> if procaine can be safely administered by the intravenous route.

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13. Gordon, R. A.: Application of Intravenous Procaine Therapy in the Surgery of Trauma, read at Congress of Anesthetists, Montreal, October 21, 1948.

# SURGICAL TREATMENT OF LOW BACK PAIN WITH SCIATIC RADIATION

Preliminary Report on Three Hundred and Forty-Six Cases

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AND

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DETROIT

**A**LTHOUGH there are already many articles on the subject of low back pain with sciatic radiation, we feel that our experiences may be worth recounting because (1) from the beginning such treatment has been a joint project of the orthopedic and neurosurgical divisions of this hospital and (2) because from it we have developed certain concepts that seem a little different from those commonly expressed in most of the other reports.

We wish to place emphasis upon three main points which we intend to make in this report. The first is that disturbances of the intervertebral disks may be but a part of a more general dysfunction involving the vertebral and related structures. We feel that these lesions which do not show frank pathologic changes in the disks should receive greater emphasis than they have in the past. The second is that we recommend uncapping of the nerves (especially the fifth lumbar) in all cases in which the disk is not the obvious compressing factor. The third is our experiences regarding fusion which have led us to maintain an intermediary position regarding its use.

Our report comprises 346 consecutive cases in which the diagnosis of "nerve compression syndrome" had been made by both divisions during the last seven years. We, by common consent, used the more general term, "nerve compression syndrome,"<sup>1</sup> because in our early experience only about 40 per cent of the cases showed frank extruded or protruded segments of disks and the rest showed various other

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From the Orthopaedic and Neurosurgical Divisions, Henry Ford Hospital, Detroit.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 19, 1949.

1. Crawford, A. S.: Nerve Compression Syndrome of Lumbar Nerves: Modern Concepts and Surgical Treatment, *J. Maine M. A.* **36**:183-188 (Nov.) 1945.

abnormalities which at first we did not correlate, but which now seem to us to fit into a definite entity. We are omitting the data on sex, age, relationship of trauma and results of spinal fluid and neurologic examinations, as they do not contribute anything not already brought out in many excellent reports published previously.

In choosing patients for operation we have tried to maintain a conservative attitude. Patients with acute conditions were treated conservatively for from two weeks to several months if there was improvement. Chronic or recurring conditions were considered surgical when the severity and duration of pain and disability seemed to warrant the more radical form of treatment.

In the majority of cases some or all of the signs and symptoms of nerve compression syndrome were present: (1) diminution of the ankle or knee jerk; (2) positive Lasègue sign with or without pain on straight leg raising; (3) hypesthesia over one or two dermatomes; (4) weakness of one or several muscle groups; (5) list of the spine; (6) muscle spasm of the lumbar region and pain on movement of the trunk; (7) tenderness on palpation over the affected lumbar facet and/or over the sciatic nerve, and (8) pain of the typical nerve root type in the distribution of the fourth or fifth lumbar and/or first sacral dermatomes.

In establishing the diagnosis we considered most carefully the history and the neurologic and roentgen findings; in 206 cases we also used myelography as corroborative of other diagnostic criteria. This was also useful in showing multiple and bilateral lesions and helped us to plan the surgical attack more intelligently.

Earlier in our experience we concentrated on the intervertebral disk and assumed that the removal of the ruptured segment was sufficient to relieve all the pain; but there were so many of our patients who reported either a return of the old pain, occurrence on the opposite side or a troublesome stiffness or ache in the back on exertion that we began trying a number of more radical procedures in the hope of curing a larger percentage of patients and of learning the reason for the failures. There were 385 operations on 346 patients (table 1). There were no deaths in the series.

It should be stated that from the beginning we have advocated adequate exposure. We found that a square-shaped interlaminar opening made with an osteotome and chisel gave better access to the disk and overlying nerve than the round window made with a rongeur. The protruding portion of the annulus was excised, and the soft, degenerated nucleus pulposus was curetted out, not too vigorously. For better removal of an extruded segment of disk, the opening was often enlarged laterally and upward. It was this part of the technic which

led us gradually to the conviction that the compression of the nerve was often due to a combination of forces—the protruded or prominent disk compressing anteriorly, and bony, ligamentous and fibrous tissue compressing from behind and laterally.

Hence our present conception of this problem is that the protruding disks are but a part of the structural dysfunction which involves any or all of the several structures that make up the various joints of the vertebral column. In some cases it is protrusion of the disk that is most evident; in others the prolapse results in bulging or swelling of the ligamentum flavum<sup>2</sup> and/or hypertrophy of fibrous tissue of the joint capsule. The downward prolapse also brings closer together the narrow walls of the intervertebral foramen.

These abnormalities are not evident unless one removes the inferior articular process and that portion of the superior articular process which overlies the nerve in the foramen. This is referred to subsequently as uncapping of the nerve. The nerve most commonly affected is the

TABLE 1.—*Operative Procedures\**

Procedure	No.
Unilateral hemilaminotomy .....	168
Bilateral hemilaminotomy .....	86
Hemilaminotomy and uncapping of nerve.....	83
Bilateral hemilaminotomy and uncapping of nerve.....	26
Bilateral laminectomy, sparing facets.....	10
Removal of neural arch.....	12
Total .....	385

\* Including 39 secondary operations.

fifth nerve, which passes through the most constricted of the foramina.<sup>2</sup> Another observation, which has been noted particularly in cases of abnormal mobility, such as spondylolisthesis and spina bifida, is that the base of the lamina which lies next to the fifth nerve at its entrance into the foramen can cause direct impingement posteriorly on the nerve, with increased extension at that joint.

Our operative experiences have shown us that it may not be enough to remove a ruptured disk segment, even though the case is clearcut; so we now routinely follow this procedure by a thorough probing outward in the foramen, feeling for any constriction or tissue which might compress the nerve. If we are not certain that there is plenty of extra space, we proceed to uncap the nerve, removing all the compressing structures. After this procedure is complete, we then cover the exposed nerve with a thin piece of fatty tissue with the hope that it will lessen the amount of fibrous tissue that will form

2. Larmon, W. A.: An Anatomic Study of the Lumbo-Sacral Region in Relation to Low Back Pain and Sciatica, *Ann. Surg.* **119**:892-896 (June) 1944.

later. Spurling and Grantham have mentioned in their recent report<sup>3</sup> that in some cases with negative findings relief was obtained by uncapping of the nerve.

In 122 of our operations nerves were uncapped as a part of the procedure. From an analysis of these cases it seems that some benefit was derived from this part of the operation. It is not possible to prove this statistically because of the several procedures combined in some of the cases, but we do feel that our results, in general, are improving, and we are inclined to give at least some credit to this procedure. As to the charge that uncapping of the nerve increases instability of the back, we know of only 2 cases in which subsequent fusion was necessary because of backache. Table 2 shows the operative findings in our cases.

The last item in table 2 includes the various structures referred to previously. Undoubtedly, some of the 73 lesser abnormalities of disks were also partly due to the other compressing structures but were not

TABLE 2.—Operative Findings

	Cases	
	No.	%
Ruptured and/or extruded disks.....	142	40
Protruding or prominent disks.....	73	20
Negative findings.....	8	2
Sclerosing osteitis (laminal thickening).....	9	38
Tumor (schwannoma) of the fifth lumbar nerve.....	1	
Other compressing structures (bony, ligamentous, fibrous, etc.)	113	
Total.....	346	

discovered at the time because in some cases the nerves were not uncapped. So it can be seen that in our series, 40 per cent were frank instances of a ruptured disk; another 20 per cent were called "prominent disks," but the condition may have been due to additional pathologic changes unrecognized at the time, and in 38 per cent it was due to compression of a nerve in or around the foramen.

It should probably be pointed out that we explored almost routinely both the fifth and the fourth lumbar disk because of the relative frequency of pathologic disks at these two sites. This was done bilaterally if in the history it was revealed that there had been trouble on both sides. Table 3 shows the relative frequency anatomically of the disks found at the operation.

As to the third point, fusion, the subject of combined operation for the nerve compression syndrome has been a controversial one for a number of years. Many papers have been written on this problem with a variety of criteria and recommendations for fusion, ranging from those

3. Spurling, R. G., and Grantham, E. G.: The End-Results of Surgery for Ruptured Lumbar Intervertebral Discs, *J. Neurosurg.* 6:57-64 (Jan.) 1949.

urging fusion in all cases to others expressing the belief that fusion is never necessary. Other observers, after thorough consideration of the problem, have concluded that there are no criteria for spinal fusion following removal of a protruded nucleus pulposus.

Inasmuch as we had so many patients with early or late return of pains in the leg and back after routine removal of a disk, we performed more and more primary fusions on a trial basis. Table 4 shows the types and number of each.

TABLE 3.—*Anatomic Location of Pathologic Disks*

Vertebra	No. of Cases
Second lumbar .....	1
Third lumbar .....	3
Fourth lumbar .....	66
Fifth lumbar .....	106
Fourth and fifth lumbar.....	38
Third, fourth and fifth lumbar.....	1

} 98%

TABLE 4.—*Fusion Operations\**

Type	No.
Albee .....	10
Modified Hibbs .....	57
Plug (iliac crest, Cloward).....	11
Facet .....	8
H type .....	11
Simple prop or strut.....	29
Total.....	126

\* Including 23 secondary operations.

TABLE 5.—*Results*

	Cases	
	No.	%
Good to excellent.....	211	61
Fair to good.....	40	12
Poor *.....	95	27
Total.....	346	

\* Including 10 failures.

Each of these methods seemed to have satisfactory results in a majority of cases. The objections to most of the methods of fusion that we have used in the past were that (1) too high a percentage of non-union resulted, (2) the period of immobilization following operation was necessarily prolonged and (3) it was difficult to establish fusion which would separate permanently the interspaces posteriorly.

Since we have utilized the prop type of graft, the results appear to have been more uniformly successful, although it is too early yet to

draw definite conclusions. The type of graft used in this method of fusion is locked securely in position and tends to keep the fourth and fifth interspaces from collapsing. The patients have been allowed up in a plaster lumbar support fourteen days after operation.

The preliminary results since the method was adopted, almost one and a half years ago, have been extremely gratifying. But it is realized that a longer follow-up period will be necessary before final conclusions can be drawn.

As to the end results in our series, we are in the process of working out a method of evaluating results which uses subjective as well as objective data. We plan to report this in a subsequent communication, but we can give the results that are recorded to date. All the patients have been followed for at least three months; some have had a follow-up period of nearly four years.

We can state that 211 patients, 61 per cent, were at work and with no complaints in from three months to over three years. This group we graded from 85 to 100 per cent, and the results were classed as good to excellent. There were 40 patients, 12 per cent, who returned to work but still had occasional trouble with the back or legs. This group we graded from 60 to 84 per cent and called the results fair to good. There were 95 patients, 27 per cent, who had more complaints than the second group. These results we considered poor. There were 10, 2 per cent, for whom results should be considered failures, although most of them are still doing some work.

In the group with poor results there were 39 reoperations on 35 patients. Of these reoperations, there were 23 fusions on 22 patients and 17 reexplorations without fusions. Of the 22 patients with secondary fusions there were 12 who had good results, 4 who had fair results and 4 who had results graded as poor; in 1 the result was a failure, and 1 did not return for examination. Of the 17 patients with nonfusion operations, 9 had good results, 2 fair, 4 poor and 1 failure; 1 was not heard from.

#### SUMMARY

We are reporting a series of 346 consecutive cases of nerve compression syndrome in which there were 385 operations.

In 40 per cent of cases frank ruptured disks were found; about 20 per cent showed less definite pathologic changes in the disk, and there were 38 per cent in which the pathologic process involved the other vertebral structures. In about 2 per cent the findings were recorded as negative.

We advocate an adequate exposure of both the fourth and the fifth lumbar disk on one or both sides according to the history, myelograms and operative findings and good surgical removal of the accessible degenerated segment of disk.



We also advocate uncapping of the nerves, at least the fifth lumbar nerve, unless one can be certain after thorough probing that the nerve is not in danger of compression in the nerve canal. In some cases of well marked disease of a disk there is also nerve compression in the foramen, which explains persistence of pain after removal of the disk.

We advocate primary fusion in cases in which there has been a long history of pain in the back or legs and in which there is roentgen or operative evidence of instability to make this procedure justifiable. We have found by experience that a strut or prop type of graft has given us the most satisfactory results. By good coordinated team work the operative time for this combined procedure can be cut down considerably, and with this type of graft, ambulation and convalescence can be shortened.

#### CONCLUSIONS

This report is intended as a statement of our combined experience and present impressions. During the last year our results have been more satisfactory as a whole than any we previously obtained. At present we feel convinced that these better results are being gained by the more careful searching for the nerve-compressing structures (disk and nondisk), uncapping of the nerves wherever indicated and primary fusion in all cases in which this seems indicated. In a subsequent report we will be in a better position to evaluate the end results. We can then see whether we are able to maintain our present concepts.

#### DISCUSSION OF PRECEDING PAPERS

DR. HERMAN E. PEARSE, Rochester, N. Y.: If you look into the antiquity of the literature, you will notice that at one time I studied the fascial planes of the neck and the mediastinum in relation to the spread of infection. Because of those observations, I should like to point out that one observation in the case reported by Dr. Gardner is unusual.

The lateral view showed air behind the pharynx in a fascial space ordinarily termed the retropharyngeal or retrovisceral space. This extends from the base of the skull to the sixth dorsal vertebra. In perforations of the upper part of the esophagus it is the path of spread of infection, and, of course, these are very common in traumatic lesions from foreign bodies or esophagoscopy. This space must be drained. It can be approached easily through the neck. On the other hand, perforations below the sixth dorsal vertebra may cause emphysema in the neck, but they ordinarily do not fill the retropharyngeal space with air. Hence I merely wish to mention that in the majority of subjects the sign presented by this patient will not be found, and one will not have roentgen evidence of involvement of the retropharyngeal space from a perforation of the esophagus at the level of the eighth dorsal vertebra.

DR. A. J. ANLYAN, Columbus, Ohio: In reviewing the etiology of spontaneous rupture of the esophagus, I think I should mention a case that was brought to my attention in Columbus.

A 56 year old woman had an abdominal operation and was duly sent down to her room under the charge of her private nurse, with a Levin tube in her stomach. The nurse proceeded to hook up her Levin tube to the oxygen tank. We were called in, and the patient had a tremendous subcutaneous emphysema. She was too sick to undergo any surgical or endoscopic measures at that time, and we just instituted complete antibiotic therapy and watched her; ten days from the date of her perforation she was home, feeling well.

DR. JOHN H. GRINDLAY, Rochester, Minn.: I do not believe that I can add much to what Dr. Condon has told you about polythene. I might say again, however, that the fibrous tissue reaction which he described about the pack is truly a very minimal reaction. He said that the thickened pleura under the pack was only about 0.5 mm. thick. I have found that the fibrous tissue layer about polythene is thickest in the first few weeks after the film has been implanted. After film has been in place longer than six weeks, the fibrous layer is very thin and when one examines it histologically there are very few cells to be seen. The layer consists of collagenous fibers all oriented in the same plane and direction, and in cases in which we have used it to fill dural defects it resembles dura very closely.

I think that the procedure Drs. Condon and Harper have proposed is a very definite contribution. I hope and believe that it will stand the test of time. Dr. O. T. Clagett and I have been working on dogs in a somewhat similar study. We have placed a sealed bag of polythene film, filled with spun glass, into the pleural cavity after pneumonectomy in order to prevent overdistention of the remaining lung. Our early results were very encouraging, but, unfortunately, the material is not tough enough to stand up more than a few months. After four to eight months a crack develops or a seam bursts, and until a means of getting a better constructed bag is found I am afraid our study is at a standstill. One of the things which has encouraged us, however, is the observation that polythene produced virtually no thickening of the pleura.

DR. CAMERON HAIGHT, Ann Arbor, Mich.: Drs. Klassen, Anlyan and Curtis have emphasized the need for biopsy of certain pulmonary lesions in which a diagnosis otherwise cannot be made. One of the factors which has hitherto retarded progress in this direction has been the fear of complications following incision of the pulmonary parenchyma in conditions of a possibly infectious nature. It is noteworthy that Dr. Klassen and his associates have not experienced any complications in their series of 50 consecutive cases. They are to be congratulated on their use of a definitive procedure to obtain a diagnosis of otherwise obscure lesions.

The use of polythene film, as recommended by Drs. Condon and Harper for the maintenance of extrapleural collapse of the lung, is presented by them because of its nonirritating qualities. In this respect it should prove to be highly desirable. Certain objections are inherent, however, in the operation of extrapleural pneumolysis because of the space which is thereby created. The collective experience of many surgeons with the introduction of foreign material in order to maintain selective pulmonary collapse has shown that any type of foreign body, including air as used in extrapleural pneumothorax, may sooner or later lead to complications. Certain materials, such as paraffin, with which we have had considerable experience at the University of Michigan, and even more so the lucite balls, with which we have had no experience, possess the disadvantage of providing an irregular, firm contour which may cause localized areas of pulmonary necrosis. The softness of polythene film should be of definite advantage in lessening the objection to the other materials. There is always the possibility in any case of

extrapleural pneumonolysis that infection of the extrapleural space may occur. In particular, tuberculous infection is the type of infection most commonly encountered in these cases. It occurred in a small percentage of our cases with paraffin filling and was usually a delayed complication, being first evident between six months and four years after operation. Principally because of this complication, collective experiences with the various types of extrapleural pneumonolysis used to date have shown that the initial enthusiasm soon dampens. This was also the case with the soft type of filling, the flexi-tissue,<sup>®</sup> used by R. C. Matson and described by him in 1942. Although polythene film possesses the particular advantage of inertness, we should not endeavor to evaluate the results until an adequate period of observation has been possible.

DR. WILLIAM TUTTLE, Detroit: My colleagues and I have used procaine hydrochloride axan anesthetic agent for about the last year and a half. We have used it in a large number of thoracic operations. We think that it has certain very definite advantages. The patients wake up quickly after the operative procedure, even though the procedure is sometimes prolonged. This is a distinct advantage because it makes possible the patients' coughing early and eliminating secretions more advantageously. We feel that they definitely have less postoperative pain. We have seen no reason not to use this type of anesthetic. In fact, we have become fond of it and feel that it is certainly much better than any type of anesthetics we have had previously for thoracic procedures.

DR. K. P. KLASSEN, Columbus, Ohio: In answer to Dr. Haight's comment I wish to state that owing to the air-tight and hemostatic stitch used in our method of pulmonary biopsy, obliteration of the pleural space occurs immediately and thus infection will not occur. I have seen no cases of tuberculous sinus following this procedure in patients with pulmonary tuberculosis.

DR. C. MCG. GARDNER, Montreal, Canada: Dr. Pearse's comment brings up a rather important point. I have had the opportunity of operating on 2 patients whose esophagi had been perforated by instrumentation, and in neither of them did interstitial emphysema occur. Nevertheless, in the group of cases reported by Ridgeway, including many of the papers on spontaneous perforation, some 40 cases in all, interstitial emphysema occurred in the vast majority, although the rupture usually occurred opposite the eighth or ninth dorsal vertebra. This puzzled my colleagues and me.

We obtained a number of esophagi from cadavers and applied intraluminal pressure, sometimes below, sometimes above. The esophagus nearly always split opposite the eighth vertebra. I believe that pus then tracks up within the esophageal wall and bursts out opposite the fifth or sixth vertebra. Whether this explains the fact that the interstitial emphysema occurs so often in these cases with spontaneous rupture, I do not know, but it is an interesting thought.

DR. IVAN B. TAYLOR, Detroit: As I said, there are three types of operations in which we used procaine, and we considered it only as an adjunct and not the chief anesthetic drug. The indication that we have used most of all was thoracic surgery. As Dr. Tuttle has pointed out, it has been found useful there, and we have about 200 cases done for Dr. Tuttle and his associates with this method. I should like to discuss more fully the anesthesia record of a first stage thoracoplasty. The patient was a woman about 35 years old. Thiopental sodium (450 mg.) was administered intravenously during induction, followed by nitrous oxide and intravenously administered procaine hydrochloride throughout the rest of the operation, which lasted less than an hour. This patient was not intubated for this

thoracoplasty. Her recovery was rapid. She was awake in five minutes, and that is not just active reflexes. The patient talked to us in five minutes and asked for fluid when she got back in the room. I told her she could have water and had a discussion with the special nurse because she had been nursing patients twenty years and "knew that they mustn't drink water after an operation." So I do not know whether it does much good to give good anesthesia; the attendants still want to treat the patients for poor anesthesia afterward. The patient had twenty minutes of complete relief from pain, was very comfortable and, of course, was able to clear out excess secretions by coughing. That is not an absolute indication, but it is one we have used most of all. For superficial operations, in which only light anesthesia is necessary, we have thought procaine was beneficial. These undesirable reflexes that we have encountered in anesthesia for years—excess salivation in light anesthesia, sweating which often occurs, cough, and so forth, things that occur in light anesthesia—have been fairly well depressed by the use of procaine hydrochloride in a 1 per cent solution. Some of these patients had as much as 2 or 3 Gm. of procaine an hour.

The patients undergoing thyroidectomy have done particularly well. Anesthesia for thyroidectomies is no longer the difficult problem that it was before the days when you didn't cool them off with propylthiouracil. I would like to try procaine on some patients with toxic thyroid disease.

PRESIDENT BISGARD: Dr. Granger?

DR. GRANGER: I have nothing to add.

## POSTOPERATIVE MANAGEMENT OF PATIENTS UNDERGOING TRANSTHORACIC GASTROESOPHAGEAL OPERATIONS

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AND

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IT WAS not many years ago that a famous American surgeon made the statement that carcinoma of the esophagus is beyond the realm of surgical therapy. It is only in recent years that malignant lesions of the cardiac end of the stomach which have invaded the lower esophagus have been completely removed by operative means. The surgeon is indebted to the tremendous advances in anesthesiology and to progress in the field of antibiotics for his opportunity to attack such lesions. They have enabled him to open the chest and mediastinum, considerably diminishing the serious dangers with which he formerly was confronted. The availability of blood in quantities sufficient to replace losses as they are encountered diminishes the danger of hemorrhagic shock. Although these advances have made transthoracic procedures on the stomach and esophagus justifiable, such operations still carry a high mortality and morbidity. Several factors are contributory. Most patients who require this type of operation are old and debilitated and have lost from 30 to 50 pounds (13.6 to 22.7 Kg.) in weight. The reluctance of the patient to visit his physician early and of his physician to institute early surgical therapy generally results in a delay of many months between the onset of symptoms and the time of operation. This is reflected in the nutritional state of the patient, in his cardiac reserve and in his ability to withstand any extensive surgical procedure which carries with it much damage to tissues, considerable hemorrhage and loss of fluid, interference with

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From the Surgical Service, Veterans Administration Hospital, Hines, Ill., and the Department of Surgery, University of Illinois College of Medicine.

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respiration and shock. In spite of these factors, this type of operation offers many persons an opportunity for months or years of added life, comfort, and happiness, instead of an inevitable early death.

The greatest dangers of postoperative mortality in transthoracic gastroesophageal operations occur in the first few postoperative days. The mortality and morbidity are in direct proportion to the energy, efficiency and judgment displayed during their postoperative management. Best results are obtained by carefully planned team work of the surgeon, anesthesiologist, nurses and residents. At all times, the patient must be under the careful observation of a person who has knowledge of the postoperative routine and who can recognize the

TABLE 1.—*Relation of Type of Operation to Complications and Deaths\**

Type of Operation	No. of Cases	Complications*		
		None	Single	Multiple
Gastroesophageal resection .....	20	6	2	12 (5)
Exploratory thoracotomy .....	6	3	3 (1)	0

\* The figures in parentheses indicate the number of deaths.

TABLE 2.—*Postoperative Complications*

Type	No.	Type	No.
<b>Pulmonary</b>		<b>Cardiovascular</b>	
Atelectasis.....	4	Cardiac failure.....	2
Edema.....	3	Thrombophlebitis.....	2
Bronchopneumonia.....	2		
Infarct.....	2	<b>Miscellaneous</b>	
<b>Thoracic Cavity</b>		Leakage at suture line.....	2
Hydrohemothorax.....	8	Subphrenic abscess.....	1
Empyema.....	2	Subcutaneous emphysema.....	1
Pneumothorax.....	1		
Hematoma of mediastinum.....	1		

early evidences of complications when they arise. A qualified surgical resident must literally "live with the patient" during the first few postoperative days. A delay in recognition and care of untoward symptoms frequently will result in the death of the patient.

Cardiovascular and respiratory complications are common and potentially serious. Similar complications have been reported by most surgeons performing these types of operations, regardless of the pre-operative preparation or the surgical technic involved. The great majority of deaths occur in the early postoperative period.

At the Veterans Administration Hospital, Hines, Ill., 26 patients have been operated on for resection of the stomach and esophagus or of the esophagus alone through the transthoracic approach. As can be seen from table 1, resections were completed in 20 patients, of

whom 5 died postoperatively. The remaining 6 patients underwent exploratory thoracotomy, but the malignant lesions were so extensive that they were inoperable. Of this group 1 patient died. Of the entire 26 patients, 9 recovered without complications. Another 5 had only one major postoperative complication. The remaining 12 had multiple complications.

The various complications encountered and their frequency are listed in table 2.

Table 3 lists the time of death and the complications which developed in each of the fatal cases.

#### POSTOPERATIVE CARE

To minimize the frequency and severity of these complications, a plan of postoperative management has been developed and is employed.

TABLE 3.—*Factors Contributing to Postoperative Mortality*

Case	Esophageal Disease	Operation	P.O. Day of Death	Complications
1	Stricture	Resection	1	Atelectasis, bronchopneumonia, pulmonary edema, hydrohemothorax
2	Carcinoma	Thoracotomy	2	Massive pulmonary edema
3	Carcinoma	Resection	1	Cardiac failure
4	Carcinoma	Resection	2	Hydrohemothorax, hematoma of mediastinum
5	Carcinoma	Resection	2	Hydrohemothorax, cardiac failure
6	Carcinoma	Resection	11	Leakage at suture line, empyema, pulmonary infarct

It may be divided into eight cardinal points. These are: (1) stir-up regimen; (2) tracheobronchial toilet; (3) suction; (4) sedatives, narcotics and analgesics; (5) oxygen; (6) fluid and nutritional balance; (7) antibiotics, and (8) recovery routine.

*Stir-Up Regimen.*—We believe physical activity on the part of the patient to be one of the most important factors of the entire postoperative management. If this is neglected, disastrous results will likely occur. The regimen consists of five features.

(a) Deep Breathing: The patient is required to take six to ten deep breaths at least every half hour. This should repeatedly be observed by a competent member of the team and should be charted.

(b) Carbon Dioxide-Air Therapy: Many patients will not breathe deeply of their own accord. This group is forced to breathe deeply by the use of pure carbon dioxide-air which is administered in the following manner. A nozzle of the carbon dioxide tank is held approximately 8 to 10 inches (20 to 25 cm.) from the patient's face and the gas permitted to flow over the patient's face during eight to ten res-

pirations unless he manifests signs of increased respiratory exchange earlier. In this way adequate aeration is maintained in most of the alveoli of the lung. Air is advantageous because of its high nitrogen content, which is less rapidly absorbed from the alveoli. Thus, if the patient coughs, air will tend to force any secretions into the tracheobronchial tree, from which they can be coughed and expectorated.

(c) *Frequent Turning from Side to Side:* The patient should be requested to turn from side to side at least every half-hour. Too frequently patients are permitted to remain on their backs for long periods, encouraging stasis and resultant pulmonary complications. This activity likewise should be recorded on the chart, which should be carefully followed by the responsible physician.

(d) *Coughing:* Coughing should be encouraged to eliminate secretions from the tracheobronchial tree. Nothing should be done which will interfere with the cough reflex. This reflex serves as a "watchdog" of the tracheobronchial tree. Patients who do not cough because of pain can be given a paravertebral block and then encouraged to cough after the pain has been relieved. This activity must be insisted on, as most patients prefer to lie quietly and maintain shallow respirations. In case no secretions are present in the tracheobronchial tree, such activity is less important.

(e) *Early Mobilization:* It has been our policy to encourage the patient to move about as soon as possible. When expedient, he is asked to sit on the side of the bed on the second postoperative day and in a chair on the third. Because of the marked debility of most of these patients, we do not encourage walking in this early stage but do desire to have them in a sitting position.

Preoperative explanation of the importance of all of these factors to the patient elicits better cooperation on his part. Postoperative explanation is on occasion not productive of cooperation because of the toxic state of the patient.

*Tracheobronchial Toilet.*—We believe that the secretions in the tracheobronchial tree should be removed immediately. The presence of such secretions is considered a respiratory emergency, and they should be removed whenever noted, irrespective of the time of day or night. It is negligent to wait for signs of atelectasis or pneumonia before removing such secretions. Two methods are used to accomplish this. An endotracheal tube may be passed, under topical anesthesia, by visible or blind technic, and through this tube a suction catheter is passed. Daily roentgen and clinical observations serve as a guide to the bronchi needing aspiration. The vigorous coughing produced by the tube is an important factor in clearing the bronchi or in raising



the secretions to a level from which they can be aspirated. Where the endotracheal tube has not produced satisfactory removal of secretions, bronchoscopy is employed. It is also employed in case there is a specific obstruction of a branch bronchus with evidence of atelectasis. Prompt and frequent aspirations of the tracheobronchial tree should minimize the development of atelectasis.

*Suction.*—Gastrointestinal: A Rawson-Abbott tube is passed through the anastomosis at the time the stoma is made and is so anchored that the suction portion will remain in the stomach while the feeding limb extends into the duodenum or jejunum. We believe it important to keep the stomach deflated for the first four or five postoperative days to prevent this organ from becoming distended and causing tension on the suture line as well as compression of the lung. It also permits early postoperative feeding through the distal lumen. Gastric atony resulting from section of the vagus nerve as well as surgical manipulation almost invariably occurs and is followed by gastric distention if suction is not employed.

Thoracic: On completion of the gastrointestinal portion of the operation, a catheter is placed in the chest through a stab wound in an area best suited for dependant drainage. The lung then is fully expanded and kept so until the chest wall is closed, at which time the catheter is connected to a water trap. The maintenance of an efficient water seal is most important and demands frequent inspection. The minimal amount of pressure necessary to prevent the inflow of air during inspirations should be maintained. This usually requires from 3 to 5 cm. of negative pressure. The inevitable oozing of blood tends to produce clots which may block the catheter. To prevent this, the drain should frequently be stripped or irrigated with a solution of penicillin. If roentgen and physical examinations indicate that pneumothorax exists, expansion of the lung may be aided by the use of a Stedman pump in connection with the water seal. Maintenance of proper suction eliminates the hazards of pleural effusion, hydrothorax and hemothorax or pneumothorax. If proper suction is maintained, we have rarely had difficulty with pleural effusion. Occasionally blood or fluid will collect in the chest which cannot be removed through the existing catheter drainage. In these circumstances, the fluid is aspirated by a syringe and large needle. If the lung is well expanded and there is little or no fluid in the chest on the fourth or fifth day, the drain is removed. If fluid or air collects within the chest after removal of the drain, thoracentesis is immediately carried out and repeated whenever indicated.

*Sedatives, Narcotics and Analgesics.*—Our observations lead us to concur in the belief that patients who have had a transthoracic esophageal operation can be “killed with kindness.” We are firmly convinced that only minimal amounts of sedatives, narcotics and analgesics should be used. During the first thirty-six postoperative hours, we administered from 50 to 100 mg. of meperidine hydrochloride (demerol hydrochloride®), as indicated. On the third postoperative day, it is rare that more than three doses of this drug are given. Opiates, barbiturates or drugs which tend to depress the cough reflex or respirations are avoided. If the patient complains of severe pain, we have relieved it by paravertebral block anesthesia. This in conjunction with small doses of demerol hydrochloride® has given satisfactory results.

*Oxygen.*—Oxygen is administered preferably by use of a BLB or similar mask with which some rebreathing takes place. This minimizes drying in the respiratory passages that frequently produces thick viscid secretions in the tracheobronchial tree which are difficult for the patient to eliminate. If a patient does not comfortably tolerate a mask, oxygen is administered by the oropharyngeal route. Oxygen tents are unsatisfactory, as they interfere with the care of these patients and the many inspections and examinations which are essential to the recognition of early complications. Such activities cannot be carried on in a tent if it is to maintain its most efficient function. Oxygen is used in the presence of tachycardia, tachypnea, cyanosis, early shock and evidences of inadequate respiratory exchange, such as atelectasis, secretions into the bronchial tree or pleural effusion. Although oxygen is not routinely used, we employ it at the slightest indication of hypoxia. Its main disadvantage is its dehydrating action on secretions in the tracheobronchial tree. Humidifiers have proved of little value to us in preventing this dehydration. Steam has the disadvantage of increasing the temperature, which, in turn, decreases the relative humidity.

*Fluids and Nutritional Balance.*—The maintenance of fluid balance is very important, but overhydration must be avoided because of the danger of pulmonary edema and an increased cardiac load. Isotonic sodium chloride solution should be used sparingly. We administer not more than 1,000 cc. on the first postoperative day and prefer to give only half that amount or less on subsequent days. Blood should be given to replace lost blood, but excessive amounts should be avoided. During the operation we administer from 1,000 to 3,000 cc. of blood, depending on the amount of bleeding encountered. Two intravenous setups with large needles are employed throughout the operation so that blood may be administered rapidly if vigorous bleeding is

encountered. In this manner, shock is avoided. The administration of whole blood and the amount employed in the postoperative period are determined by the amount of serosanguineous drainage from the pleural cavity and the clinical and laboratory indications of anemia. It is seldom if ever administered purely for its nutritional value, especially if the cardiac reserve of the patient is minimal.

The poor nutritional state of the great majority of these patients demands the early administration of food elements, particularly protein. A Rawson-Abbott tube permits the early drip feeding of solutions containing large amounts of proteins, carbohydrates and vitamins B, C and K. Such feedings are generally begun on the second or third postoperative day. Food elements which will coagulate or curd, such as milk, should be avoided, as they may be regurgitated into the stomach and block the holes on the suction portion of the Rawson-Abbott tube, with resultant gastric distention.

*Antibiotics.*—Antibiotics have been of inestimable value in the prevention of infection in patients undergoing transthoracic and mediastinal operations. However, we mention them far down on our list of cardinal points of postoperative care because their use does not replace or minimize the importance of the foregoing factors. Without proper attention to these factors, antibiotics will not prevent a high mortality. They can be relied on to retard the development of infection. Penicillin is given for several days preoperatively and postoperatively until the danger of infection is passed. This drug is administered intramuscularly and is used in solution for irrigation of the pleural cavity through the drainage catheter. Recently we have been using it by nasal inhalations in preoperative preparation. Streptomycin and sulfonamide drugs also are utilized when indicated.

*Recovery Routine.*—The establishment of a recovery room has greatly facilitated the postoperative care of all patients who have undergone major surgical procedures, particularly those having transthoracic operations. Both nursing and attending personnel have been trained and are familiar with all details of our postoperative regimen. The surgeon and the anesthesiologist are equally responsible for the care of the patient and work in harmony. They must be familiar with all details of postoperative therapy and must remain in constant attendance. Their diligence is the greatest factor in successful postoperative treatment.

#### SUMMARY

Transthoracic surgical procedures on the stomach and esophagus offer some measure of hope to many patients who, until recent years, were doomed to an early death from their disease or from starvation.

Although the incidence of cure of malignant diseases of these organs is not high, surgical intervention reestablishes continuity of the lumen of the gastrointestinal tract and permits these patients to eat food normally and to maintain their health and strength, often for many months or years. Because these patients are elderly and debilitated and in a poor nutritional state, and because the operation required to remove their disease is extensive, traumatic and shocking, the postoperative mortality will be high unless unusual care and diligence are exercised in their postoperative management. The factors which we believe to be important in postoperative therapy of patients who have undergone transthoracic esophageal operation are outlined and discussed.

# GANGRENOUS PERFORATION OF THE GALLBLADDER

Analysis of Nineteen Cases

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IT IS NOW one hundred and five years since James Duncan,<sup>1</sup> surgeon at the Royal Infirmary in Edinburgh, cited a case of gangrene of the gallbladder with perforation, followed by peritonitis and death. The conditions were observed at autopsy. In 1894, fifty years following Duncan's observation, Hotchkiss<sup>2</sup> reported the first case in which operation was performed. In 1895, W. J. Mayo<sup>3</sup> reported the first successful removal of a gangrenous gallbladder. Since that time many reports have been published.

Gangrene of the wall of the gallbladder is complete necrosis of a portion of the wall in one or more areas. Gangrene of a portion of the gallbladder wall, followed by perforation, is a sequel of acute cholecystitis. The term does not imply that the entire gallbladder is gangrenous.

This report deals with 19 cases of gangrenous perforation of the gallbladder which fall into types 1 and 2 of the Niemeier<sup>4</sup> classification: acute free perforation and subacute pericholecystic abscess. Niemeier type 3, internal biliary fistula, is not included in this study.

## INCIDENCE

This series of 19 gangrenous perforations of the gallbladder were found at operation (table 1). These cases extend over a period of twenty-one years (1928-1949), and the operations were done by sur-

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From the Departments of Surgery, St. Luke's Hospital and the University of Illinois College of Medicine.

1. Duncan, J.: Femoral Hernia: Gangrene of the Gall Bladder, Extravasation of the Bile, Peritonitis, Death, *North J. Med.* **2**:151-153, 1844-1845.

2. Hotchkiss, L. W.: Gangrenous Cholecystitis, *Ann. Surg.* **19**:197-205, 1894.

3. Mayo, W. J.: Some Observations on the Surgery of the Gall Bladder and Bile Ducts, *Ann. Surg.* **30**:452-458, 1899.

4. Niemeier, O. W.: Acute Free Perforation of the Gall Bladder, *Ann. Surg.* **99**:922-924 (June) 1934.

TABLE 1.—Incidence of Perforated Gallbladders

Author	Total Cases Re-viewed	Total Cases of Acute Cholecystitis	No. of Cases with Perforation	% of Total Cases with Perforation	% of Acute Cases with Perforation	Mortality in Cases with Perforation
Fifield, L. R.: Brit. M. J. 2: 635, 1926.....	1,066	153	28	2.6	....	43.0
Heuer, G. J.: Ann Surg. 99: 881, 1934.....	800	106	23	2.8	21.0	34.7
Stone, W. W., and Douglas, F. M.: Am. J. Surg. 45: 301, 1939.....	775	170	17	2.1	10.0	5.8
Mentzer, S. H.: Surg., Gynec. & Obst. 62: 879, 1936 .....	149	51	18	12.0	23.5	27.7
Edwards, C. R.; Gerwig, W. H., and Guyton, W. L.: Ann. Surg. 113: 824, 1941.....	1,124	194	21	1.8	10.8	28.5
Wallace, R. H., and Allen, A. W.: Arch. Surg. 43: 763 (Nov.) 1941.....	2,273	415	64	2.8	15.4	17.2
Diffenbaugh, Sarver and Strohl, 1949.....	1,127	75	19	1.6	25.3	21.5
Total.....	7,314	1,164	190	2.5	16.3	29.5

TABLE 2.—Incidence of Perforations in All Types of Acute Cholecystitis as Collected from the Literature

Author	Total No. of Cases of Acute Cholecystitis	No. of Cases with Perforation	% of Acute Cases with Perforation	Mortality in Cases with Perforation
Fifield, L. F.: Brit. M. J. 2: 635, 1926.....	153	28	18.0	43.0
Graham, H. F.: Ann. Surg. 93: 1152, 1931.....	198	10	5.0	5.0
Pratt, G. H.: Am. J. Surg. 22: 46, 1933.....	120	3	2.5	33.3
Heuer, G. J.: Ann. Surg. 99: 881, 1934.....	106	23	21.0	34.7
Mentzer, S. H.: Surg., Gynec. & Obst. 62: 879, 1936.....	51	18	23.5	27.7
Heuer, G. J.: New York State J. Med. 36: 1643, 1936.....	126	13	11.0	15.3
Pennoyer, G. P.: Ann. Surg. 107: 543, 1938.....	300	61	20.3	13.1
Graham, H. F., and Hoefle, M. D.: Ann. Surg. 108: 874, 1938 .....	100	4	4.0	75.0
Totten, H. P.: Am. J. Surg. 41: 29, 1938.....	100	20	20.0	10.0
Estes, W. L., Jr.: Am. J. Surg. 40: 197, 1938.....	78	9	11.5	2.08
Stone, W. W., and Douglas, F. M.: Am. J. Surg. 45: 301, 1939 .....	170	17	10.0	5.8
Hotz, R.: Am. J. Surg. 44: 706, 1939.....	574	69	12.1	26.1
Koster, H., and Kasman, L. P.: Am. J. Digest Dis. 6: 373, 1939 .....	341	33	9.7	27.2
McCloskey, J. F., and Lehman, J. A.: Rev. Gastroenterol. 7: 176, 1940 .....	68	12	17.6	16.6
Atlee, J. L., and Atlee, J. L., Jr.: Pennsylvania M. J. 44: 731, 1941 .....	193	16	7.7	18.8
Frankel, H.; Abramson, E., and Berk, J. E.: Rev. Gastroenterol. 8: 481, 1941.....	100	18	18.0	30.7
Edwards, C. R.; Gerwig, W. H., and Guyton, W. L.: Ann. Surg. 113: 824, 1941.....	194	21	10.8	16.6
Wallace, R. H., and Allen, A. W.: Arch. Surg. 43: 762 (Nov.) 1941 .....	415	64	15.4	17.2
Glenn, F., and Moore, S. W.: Arch. Surg. 44: 677 (April) 1942 .....	350	25	7.1	12.0
McLanahan, S.; Trout, H., Jr., and Weary, W.: Am. J. Surg. 56: 432, 1942.....	140	14	10.0	42.8
Schaeffer, R. L.: Pennsylvania M. J. 45: 566, 1942.....	122	20	16.0	40.0
Hauk, G. W.: Pennsylvania M. J. 45: 566, 1942.....	131	17	12.9	11.7
Wesson, H. R.: Proc. Staff Meet., Mayo Clin. 12: 500, 1943	76	16	21.0	12.5
Blumberg, N., and Zisserman, L.: Am. J. Surg. 70: 38, 1945	82	21	25.0	33.3
Bachhuber, C. A.; Deeb, P. H., and Taylor, E. A.: Am. J. Surg. 67: 40, 1945.....	804	55	6.8	42.4
Johnstone, G. A., and Ostendorf, J. E.: Arch. Surg. 53: 1 (July) 1946 .....	105	3	2.8	0
Diffenbaugh, Sarver and Strohl (1949).....	75	19	25.3	21.5
Totals.....	5,272	630	11.9	23.8

geons of one service at St. Luke's Hospital. During these twenty-one years, there were 1,127 operations on the gallbladder, with 19 cases of Niemeier's types 1 and 2 perforations. This is an incidence of 1.69 per cent. Of these 1,127 operations, 75, or 6.65 per cent, were for acute cholecystitis. By acute cholecystitis we mean pathologically confirmed acute inflammation of the gallbladder wall. An extensive review of the literature reveals perforations in 11.9 per cent of 5,272 cases of acute cholecystitis. The mortality rate following perforation in this collected series of acute cholecystitis was 23.8 per cent (table 2). The incidence of 25.33 per cent of perforations in pathologically confirmed acute cholecystitis at St. Luke's Hospital, Chicago, prompted this study.

#### AGE

The youngest patient was a man aged 29; the oldest, a woman aged 79 (table 3). The average age of the 10 women was 58.6 years and

TABLE 3.—*Age Incidence*

Age, Yr.	Cases, No.	Percentage
20-29.....	1	5.2
30-39.....	4	21
40-49.....	1	5.2
50-59.....	4	21
60-69.....	2	10.5
70-79.....	7	37

of the 9 men 56.0 years. The average age of the total group was 57.2 years. Four patients, or 21 per cent, were between 30 and 39 years of age, and 13, or 68.5 per cent, were over 50.

#### SEX

Ten, or 52.6 per cent, of the patients were women, and 9, or 47.3 per cent, were men. Of the 13 patients past 50 years of age, 6 were men and 7 were women.

#### DURATION OF PRESENT ILLNESS

Sixteen perforations of the gallbladder, or 84 per cent, occurred between twelve and seventy-two hours after the onset of symptoms (table 4). In 3 cases, or 16 per cent, the present illness extended over a three to six day period. In Cowley and Harkins'<sup>5</sup> series of 25 cases, 9 perforations, or 36 per cent, occurred within the first thirty-six hours.

5. Cowley, L. L., and Harkins, H. N.: Perforation of the Gall Bladder, Surg., Gynec. & Obst. 77:661-668 (Dec.) 1943.

## DURATION OF HISTORY OF PREVIOUS ATTACKS

Sixteen patients, or 84 per cent, gave a history of previous disease of the gallbladder. In 11 patients, or 57.8 per cent, the disease extended over a period of from two to more than ten years. It is interesting to note that in 3 cases, or 16 per cent, no history of previous disease of the gallbladder was obtained.

## SYMPTOMS

Pain in the right upper abdominal quadrant was present in all 19 cases (table 5). Nausea was present in 11 cases and vomiting in 10. In 3 cases there was generalized abdominal pain. Chills and fever

TABLE 4.—*Duration of Present Illness*

Duration of Illness, Hr.	Cases, No.	Percentage
12-24.....	9	47
24-72.....	7	37
72-144.....	3	16

TABLE 5.—*Symptoms*

Symptoms	Cases	
	No.	%
Pain in right upper quadrant.....	19	100
Nausea.....	11	60
Vomiting.....	10	58
Generalized abdominal pain.....	3	16
Chills and fever.....	3	16

were present in 3 cases; at operation, in these 3 cases stones were found in the common duct.

## LABORATORY DATA

The leukocyte count was of little significance in demonstrating the presence of perforation of the gallbladder. In 9 cases (47 per cent) the leukocytes numbered more than 20,000; in 3 cases (16 per cent) they ranged between 10,000 and 15,000, in 4 (21 per cent) between 6,000 and 10,000 and in 3 between 15,000 and 20,000.

## TEMPERATURE

Fifteen patients, or 78.9 per cent, had rectal temperatures between 101.6 and 103 F. Two patients, or 10.5 per cent, had rectal temperatures of 98.6 and 100 F.; 1 or 5.2 per cent, of from 100 to 101.6 F. and 1 above 103 F.



## PHYSICAL FINDINGS

Tenderness in the right upper abdominal quadrant was present in all 19 cases (table 6); a mass was palpable in 10 (58 per cent) and jaundice was present in 4 (21 per cent).

## PREOPERATIVE DIAGNOSIS

In 13 cases, or 70 per cent, the diagnosis of perforation of the gallbladder was made preoperatively. It should be pointed out again that these 19 cases were from the same surgical service; there have been continuity and overlapping of attending surgeons throughout the years

TABLE 6.—*Physical Findings*

Physical Findings	Cases	
	No.	%
Tenderness in right upper quadrant.....	19	100
Mass in right upper quadrant.....	10	58
Jaundice.....	4	21
Shock.....	1	5

TABLE 7.—*Grouping According to Niemeier Classification*

Classification	Cases		Deaths, Mortality,	
	No.	%	No.	%
Type 1, acute free perforation.....	7	35.0	2	29.0
Type 2, pericholecystic abscess.....	12	60.0	2	17.0
Total.....	19	....	4	Over-all Mor- tality, 21%

covered by this study, and consultations among the members of this service are frequent.

## GROUPING ACCORDING TO NIEMEIER CLASSIFICATION

In 7 cases, or 35 per cent, the perforations were of the Niemeier type 1, or acute free perforations (table 7). There were 2 deaths in this group, a mortality rate of 29 per cent. In 12 cases, or 60 per cent, the perforations were of the Niemeier type 2, or pericholecystic abscess. There were 2 deaths in this group, a mortality rate of 17 per cent. Four deaths in 19 cases represents an over-all mortality rate of 21.5 per cent.

## TYPE OF OPERATION

In 11 cases, or 57.8 per cent, the gallbladder was removed (table 8). On 2 occasions stones were found in the common duct, and drain-

age of the common duct was instituted at the time of cholecystectomy. On 1 occasion the appendix was removed at the time of cholecystectomy.

In 8 cases, or 42 per cent, drainage of the gallbladder was carried out. On 1 occasion, stones were found in the common duct, and drainage of the common duct was done at the time of cholecystostomy.

#### LENGTH OF STAY IN THE HOSPITAL

The average stay in the hospital of the 15 patients who recovered was 31.5 days.

#### ANALYSIS OF THE DEATHS

Three of the 4 deaths in this series were due to sepsis and peritonitis.

One patient, a 35 year old woman, died on the forty-seventh postoperative day. The duration of symptoms before operation in this case was twenty-four

TABLE 8.—*Type of Operation*

Type of Operation	Cases	
	No.	%
Cholecystectomy.....	8	42.0
Cholecystectomy and choledochotomy.....	2	10.5
Cholecystectomy and appendectomy.....	1	5.2
Cholecystostomy.....	7	37.0
Cholecystostomy and choledochotomy.....	1	5.2

hours. Drainage of the gallbladder had been performed elsewhere three months previously. At autopsy there were many intra-abdominal abscesses, cholangitis, abscesses of the abdominal wall and abscesses of the right breast.

A 71 year old man died suddenly on the fifth postoperative day. The duration of symptoms in this case was forty-eight hours. He gave no history of previous gallbladder disease. Autopsy was not done. The clinical diagnosis of the cause of death was coronary occlusion.

A 55 year old woman died on the second postoperative day. Operation revealed a gangrenous perforation with pericholecystic abscess, free bile in the peritoneal cavity and stones in the common duct. Peritonitis was given as the cause of death.

A 56 year old woman, with severe diabetes mellitus, died twenty-four hours postoperatively. Her temperature rose to 106 F. and the pulse rate to 160. The diabetes had been poorly controlled for several days prior to her admission to the hospital. She gave a history of known gallbladder disease, with intermittent chills and fever, of one year's duration. At operation the gallbladder and an abscess were drained. Free bile and pus were found in the abdomen. Peritonitis was given as the cause of death.

All deaths occurred prior to the use of chemotherapeutic agents or antibiotic drugs in this hospital.

## COMMENT

Gangrenous perforations of the gallbladder are not infrequent abdominal emergencies. The mortality rate of 21.5 per cent in this series and 23.8 per cent in a series of 630 perforations collected from the literature emphasizes the seriousness of the condition.

Eliason and McLaughlin<sup>6</sup> stated that "a correct diagnosis of a perforated gallbladder is quite unusual." This statement is corroborated by Sanders<sup>7</sup> who reported a correct diagnosis in 4 of 46 cases. Cowley and Harkins<sup>8</sup> reported a correct diagnosis in 3 of 25 cases. From our study, we note that there is little on which to base a diagnosis of impending perforation. Furthermore, tenderness, pain and a palpable mass in the upper part of the abdomen are common conditions in many cases of acute cholecystitis.

In this series, the disease seemed progressive, which is a helpful factor in the differential diagnosis. We believe that frequent observations of the patient and his progress are of major importance in the proper evaluation of major abdominal emergencies. A careful history, accurate physical examination and evaluation of laboratory data in terms of the clinical picture, with an appreciation of the frequency with which gallbladders perforate, should lead to a greater number of correct diagnoses.

## SUMMARY AND CONCLUSIONS

A series of 19 cases of gangrenous perforation of the gallbladder is reviewed. The cases occurred during a twenty-one year period, 1928 to 1949. During this period a total of 1,127 operations on the gallbladder were performed. In 75 cases, pathologically confirmed acute cholecystitis was present. The incidence of perforated gallbladders occurring in patients undergoing all types of operations on the gallbladder in this series was 1.69 per cent. The incidence of perforated gallbladders in patients with acute cholecystitis was 25.33 per cent.

Of the 19 perforated gallbladders, 7 were of the Niemeier type 1, acute free perforation. Twelve perforations were associated with pericholecystic abscesses, Niemeier type 2.

Four deaths occurred in the 19 cases reported, a mortality rate of 21.5 per cent.

There were no distinctive signs, symptoms or laboratory findings to establish the diagnosis of impending or actual perforation of the gallbladder. Localized pain and tenderness in the right upper quadrant,

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6. Eliason, E. L., and McLaughlin, C.: Perforation of the Gall Bladder, *Ann. Surg.* **99**:914-921 (June) 1934.

7. Sanders, R. L.: Perforations of the Gall Bladder; Analysis of Forty-Six Cases, *Surgery* **1**:949-958 (June) 1937.

with the presence of a localized mass, associated with clinical and laboratory evidence of persistence or progression of the process, indicated the diagnosis in most instances.

Analysis of the 4 deaths revealed that 3 resulted from progression of sepsis secondary to the perforation. The remaining death followed an acute coronary occlusion on the fifth postoperative day.

In 16 cases, or 84 per cent, perforation of the gallbladder occurred in eighteen to seventy-two hours after the onset of symptoms.

Symptoms of previous gallbladder disease were present in 16 cases, or 84 per cent.

In view of the frequency of gangrenous perforation in acute cholecystitis (25.3 per cent) and the high mortality of gangrenous perforation (21.5 per cent), we conclude that operation should be done when there is evidence of progression of the disease during the first forty-eight hours following the onset of symptoms.

## ADEQUATE SUBTOTAL GASTRIC RESECTION FOR DUODENAL ULCER

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AND

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THE LITERATURE since 1946 has abounded with reports and discussions concerning the merits and complications of vagotomy for duodenal ulcer. We do not propose to present definite opinions regarding the procedure, since we have had no experience with the operation. The summaries and conclusions reached by others are available to all for study, and, since the majority of investigators have reported favorably, we who have resorted exclusively to subtotal resection must pause and carefully consider the longer term results of the latter operation.

Visick,<sup>1</sup> of England, in reporting 505 resections for peptic ulcer, of which 357 were for duodenal ulcer, has stated that "only by carefully following all patients and assessing their condition by independent tribunal can we gain a true picture of the effectiveness of any procedure."

Crile<sup>2</sup> has pointed out that the results of resection have left much to be desired. Extensive resections are often followed by inability to gain weight or by the dumping syndrome. Less radical resection may be followed by marginal ulcer in up to 6 per cent of cases. Contrariwise, vagotomy as reported in other series has been followed by such untoward symptoms as retention, diarrhea, bloating, belching of foul gas, nausea and weakness. Recurrence of the ulcer has also been reported.

Our series of resections is small, for we feel, as did Jordan,<sup>3</sup> that radical surgical intervention, even if productive of good results, should be done only with impelling indications. One wonders when studying the reports of large series of vagotomies whether the indications have been as definite in all cases. The relative ease of performance of the

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From The Department of Surgery, Duluth Clinic.

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1. Visick, A. H.: *Lancet* **1**:505-544 (April 3) 1948.

2. Crile, G., Jr.: *S. Clin. North America* **28**:1123 (Oct.) 1948.

3. Jordan, S.: End Results of Radical Surgery of Gastrointestinal Tract as Seen by Gastroenterologist, *J. A. M. A.* **116**:586-590 (Feb. 15) 1941.

operation and the lessened mortality rate might induce patients with mild complications to accept vagotomy earlier in the course of their disease, whereas many hesitate to submit to resection until their discomfort drives them to seek any relief offered. Our discussion, then, concerns itself solely with those patients who have had resection for real complications and seeks to answer two questions: 1. Is the patient free of his disease? 2. Is the patient comfortable.

In the past five years we have performed resection for benign peptic ulcer in 201 cases, of which 121 were cases of duodenal ulcer. The ratio of male to female patients is about 5.3 to 1 as is shown in table 1. The average age at operation is about equal in the two sexes.

TABLE 1.—*Sex and Age*

Sex	Number of Patients	Average Age in Years
Male.....	102	45.6
Female.....	19	42.1
Total.....	121	

TABLE 2.—*Previous Operations*

Operation	Number of Operations
Acute perforation.....	15 (1 marginal ulcer)
Gastroenterostomy.....	6
Pyloroplasty.....	6
Exploratory.....	2
Gastric resection.....	1
Billroth no. 1.....	1
Vagotomy.....	1
Total.....	32*

\* 32 operations in 28 patients, or 23 per cent of patients.

Twenty-eight patients, or 23 per cent of the series, had had previous operations, as is noted in table 2. The majority of these operations were for closure of an acute perforation, with gastroenterostomy and pyloroplasty next in frequency. Vagotomy had been performed in 1 instance, this operation having been done elsewhere.

All our patients have been thoroughly studied by the department of internal medicine prior to operation, and all have been given adequate trials of conservative therapy. The indications for operation have been persistent and severe pain, obstruction and hemorrhage or any combination of these three, all unrelieved by adequate and careful medical therapy. All cases, therefore, represent the real complications of duodenal ulcer, and the average duration of symptoms has been many

years. Table 3 shows that pain was present in 98 patients, hemorrhage in 27 and obstruction in 30. In many patients more than one symptom was present. The average duration of symptoms was about 11.4 years. In 1 patient, symptoms had been present for thirty-three years.

Our concept of adequate gastric resection is not new. We attempt to remove the ulcer, or, when this is unduly hazardous—as when an ulcer lies in close proximity to the common duct or is involved in a great deal of scar tissue—to exclude it. We resect at least two thirds to three fourths of the stomach, including the lesser curvature up to the esophagus, or as near thereto as possible, and perform retrocolic or antecolic gastrojejunostomy, using a short proximal jejunal loop. The anastomosis is of the open type and is followed by thorough peritoneal toilet. With the routine preoperative use of succinylsulfathiazole (sulfasuxadine®), phthalylsulfathiazole (sulfathalidine®) or phthalylsulfacetimide (thalamyd®) and gastric lavage, we have not had cause

TABLE 3.—*Symptoms\* and Average Duration in Years*

Symptom	No. of Cases
Pain.....	98
Hemorrhage.....	27
Obstruction.....	30
Average duration in years.....	11.4

\* In many cases, more than one symptom was present.

to abandon the open operation. Recently penicillin has been administered to the patients for one or two days preoperatively. An indwelling nasal suction tube is always pulled through the anastomosis and placed well within the proximal jejunal loop and, thence, into the duodenum. Since we have added this protection to closure of the duodenal stump with silk sutures, blowout has not occurred. Buttressing of the duodenal stump against the pancreas has been abandoned. In 1943 and 1944, the anterior Polya operation was done in the majority of cases. Since 1944, the Hofmeister procedure has been the operation of choice. It should be mentioned that the Finsterer exclusion procedure with excision of the antral mucosa was done in 11 cases but has not been performed since September 1946.

The immediate postoperative complications which developed in 20 cases, or 16 per cent, are shown in table 4. These represent all the postoperative complications in the series and, for the most part, are relatively minor. Under pulmonary complications we have grouped atelectasis and pleurisy. The wound infections have, for the most part, been trivial infections of the nature of minor stitch abscesses, except

for 1 case in which evisceration occurred. Prompt secondary closure in this patient resulted in recovery without further incident. Two patients required reoperation because of stomal obstruction and retention, and it is of interest to note that in both cases the closed anastomosis had been done; the last such case occurred in 1945.

There were 7 deaths in the entire series of 201 cases, or a mortality rate of 3.4 per cent. In the group with duodenal ulcer there were 6 deaths, 3 of which we feel were not directly attributable to surgical error.

TABLE 4.—*Immediate Postoperative Complications*

Complication	Number of Cases
Pulmonary.....	6
Wound infection.....	6
Retention.....	2
Hemorrhage.....	2
Subphrenic abscess.....	2
Pelvic peritonitis.....	1
Intestinal obstruction.....	1
Total.....	20 (16% of cases)

TABLE 5.—*Postoperative Deaths and Causes*

Case No.	Cause	Interval, Days	Autopsy
1	Peritonitis (3 previous operations on stomach)...	1½	Yes
2	Duodenal leak; hemorrhage.....	18	Yes
3	Perforation at anastomotic line; hemorrhage....	21	Yes
4	Psychosis; acute depression.....	8	Yes; autopsy did not show cause of death
5	Pulmonary embolus.....	9	Yes
6	Uremia (clinical).....	12	No

Table 5 lists the causes of death. The mortality rate in the series with duodenal ulcer is, thus, 4.9 per cent; excluding the last 3 cases, the rate is reduced to 2.4 per cent. In cases 2 and 3 faulty suture technic was probably to blame for the fatalities. Case 4 was that of a woman who, in a period of very acute depression predicted her own death. Death occurred on the eighth postoperative day, but autopsy did not show the cause of death. The peritoneal cavity was clean, and all the suture lines were completely intact. In case 5, sudden death occurred as a result of pulmonary embolus on the day of the patient's anticipated discharge from the hospital. Since August 1947, 74 consecutive resections for peptic ulcer have been performed without fatality and with only 1 serious complication.



Some months ago in an attempt to evaluate our results, we sent a questionnaire to all patients subjected to resection for duodenal ulcer since January 1943. Six cases have been lost to follow-up through post-operative deaths. Five cases have been lost through late deaths, three to five years after operation, but in no instance was the death in any way related to the gastrectomy. In 10 cases there has been no reply to the questionnaire. Returns have been secured in 100 cases, or 90 per cent; these 100 cases furnish the material for this report.

A reproduction of the questionnaire which was sent out accompanies this article. By means of it, we attempt to enumerate the commoner postgastrectomy symptoms to permit the patient to evaluate his own personal result on the basis of the questions listed. Our patients are seen postoperatively at one month intervals for six months and twice a year thereafter. At each office visit, the patient's status is evaluated by the surgeon and the internist. Gastrointestinal roentgen study is performed in the majority of instances, usually within six months after

TABLE 6.—*Cases Available for Study*

Total operations.....	121
Postoperative deaths.....	6
Late deaths.....	5
Lost to follow-up.....	10
Total not followed.....	21
Available for follow-up.....	100

the operation. While the degree of acidity is not measured in all cases postoperatively, about one half the patients have had test meal studies, and in only 1 instance has achlorhydria been absent. All patients are routinely placed on a rather restricted diet for six to eight weeks. Thereafter they are instructed to eat whatever foods they desire. If any food causes distress, we merely advise the patient to eliminate that item from his diet. Foods not tolerated well appear to be fried or spicy foods, chocolate, pork, cabbage, onions and coffee. Alcohol and tobacco in moderation are not forbidden. We have felt that, in addition to the regular follow-up, an analysis of the patient's answer to the questions enumerated in the questionnaire, plus giving the patients themselves an opportunity carefully to evaluate their status, would enable us to assess the result with a good degree of accuracy in almost every instance. We have not changed the evaluation placed on his result by any patient, even though symptoms listed by him may have been very vague or mild.

Uniformly, the highest percentage of excellent or good results was obtained in that group subjected to resection because of obstruction with or without pain. In 30 such cases the results were excellent or good,

except in 1 instance in which the result was evaluated by the patient himself as only fair. There were no poor results in this group.

Less satisfactory results were apparent in the group offering intractable pain or pain with hemorrhage as the operative indication. Of 70 patients in this group, 13, or 18 per cent, had fair or poor results. It would seem from an analysis of other studies that in this group

TABLE 7.—Results According to Operative Indication

Indication	Result		
	Excellent or Good	Fair	Poor
Obstruction with or without pain.....	29	1	0
Pain alone or with hemorrhage.....	57	8	5
Total.....	86	9	5

### Questionnaire

1. Are you able to eat any and all foods?  
Yes..... No.....
2. If some foods cause you distress, indicate which foods.....
3. Do you have any of the following stomach symptoms? Check which ones.
  - a. Pain..... After meals.....
  - b. Vomiting.....
  - c. Nausea.....
  - d. Bleeding.....
  - e. Feeling of fullness.....
  - f. Belching.....
  - g. Diarrhea.....
  - h. Constipation.....
  - i. Loss of appetite.....
  - j. Any others.....
4. Have you returned to work?.....
5. Can you do a full days work?.....
6. Present weight.....
7. Do you think your result from operation is
  - a. Excellent.....
  - b. Good.....
  - c. Fair.....
  - d. Poor.....

vagotomy may prove to be a better procedure. In many of these cases, however, we found subacute or chronic perforation of a posterior ulcer into the pancreas, and one wonders whether any operation short of actual excision or exclusion of the ulcer will result in permanent cure.

Table 8 shows the end results as evaluated by the patient's own answers to the questionnaire. It will be seen that 86 per cent had excellent or good results; 9 per cent, fair, and only 5 per cent have reported a poor result.

The so-called "dumping syndrome" has occurred to our knowledge in only 3 patients, and of these, 2 have experienced relief over periods of from one to four years. Nausea alone has occurred in about 8 per cent of cases, this varying from very mild occasional nausea to a somewhat more distressing and permanent symptom. Nausea and vomiting together have occurred in about 8 per cent of cases, and here again

TABLE 8.—*Results in 100 Cases with Follow-up*

Result	Number of Cases	Percentage of Cases
Excellent or good.....	86	86
Fair.....	9	9
Poor.....	5	5
Total.....	100	100

TABLE 9.—*Occurrence of Postgastrectomy Symptoms*

Symptom	Number of Cases	Percentage of Cases
"Dumping" .....	3	3
Nausea alone.....	8	8
Nausea and vomiting.....	8	8
Marginal ulcer * .....	1	1
Failure to gain weight.....	10	10

\* The patient claims an excellent result, but a roentgenogram reveals a questionable marginal ulcer. This is the only patient in the series with high free hydrochloric acid level postoperatively.

TABLE 10.—*Results According to Type of Operation*

Result	Polyn		Hofmeister	
	Number of Cases	Percentage of Cases	Number of Cases	Percentage of Cases
Excellent or good....	24	86	62	86
Fair.....	2	7	7	10
Poor.....	2	7	3	5

the symptoms, for the most part, have been transient and rather vague. Marginal (stomal) ulcer is thought to be present in only 1 case, and here the only evidence is a questionable roentgen defect of the stoma; the patient himself has only minor complaints. Of the cases with post-operative test meal studies, this is the 1 case in which achlorhydria was not produced. Failure to gain weight has occurred in 10 per cent of the cases.

Table 10 shows the results according to the type of operation, and our figures seem to indicate that the type of operation makes little difference as to end results provided an adequate resection is performed.

## SUMMARY

One hundred and twenty-one cases of adequate gastric resection for chronic, complicated duodenal ulcer are reported.

A mortality rate of 4.9 per cent would appear to be unduly high, but eliminating 3 cases in which death was not felt due to error in surgical technic, the rate becomes 2.4 per cent. Postoperative complications occurred in 16 per cent.

Excellent and good results have been secured in 86 per cent of cases, the fair or poor results occurring in that group of patients subjected to resection for persistent pain or pain with hemorrhage. In 1 case, gastrointestinal roentgen studies suggests marginal (stomal) ulcer; the patient has only minor complaints not at all suggestive of marginal ulcer.

Distressing postgastrectomy symptoms have occurred in a small percentage of patients; in many of these, symptoms have abated over a period of years.

# VON HABERER-FINNEY GASTRECTOMY WITH VAGOTOMY

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AND

JAMES BARRON, M.D.

DETROIT

WHEN BILLROTH performed the first successful partial gastrectomy in 1881, he restored intestinal continuity by anastomosing the stump of the stomach to the end of the duodenum. He was, indeed, the father of gastric surgery; for all thirty-seven different methods (Polya<sup>1</sup>) of reestablishing the gastrointestinal tract after partial removal of the stomach are modifications either of his original operation, gastroduodenostomy (Billroth I), or his subsequent procedure, gastrojejunostomy (Billroth II, 1885). Contemporaries of Billroth followed his first technic or devised modifications of their own, but modern gastric surgeons have tended to practice some variation of the Billroth II operation. The swing away from gastroduodenostomy to gastrojejunostomy occurred because the latter proved to be a safer operation. The difficulty in end to end anastomosis of the stomach and duodenum is due chiefly to inequality in size of the openings. That this was a real problem in the early days of gastrointestinal surgery is evidenced by the many modifications advocated and by constant reference in the surgical literature of that period to the dangerous upper angle, or "angle of sorrows."

The large number of marginal, or jejunal, ulcerations that followed short circuiting in the treatment of complicated duodenal ulcers led to the abandonment of this type of operation. Substitution of partial or subtotal gastrectomy has reduced the number of marginal ulcers, but the incidence is still high. Over the years many surgeons have reverted to the Billroth I type of operation on the ground that it is more physiologic and that the duodenum is better endowed by nature to withstand the often undiluted acid gastric secretions. Schoemaker was one of the first to free himself from the Billroth I prejudice.<sup>2</sup> He

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From the Department of Surgery, the Henry Ford Hospital.

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1. Polya, E.: Re-Establishment of the Gastro-Intestinal Passage after Gastric Resection, *Surg., Gynec. & Obst.* **70**:270-290, 1940.

2. (a) Mayo, W. J.: Radical Operations on the Stomach with Especial Reference to Mobilization of the Lesser Curvature, *Surg., Gynec. & Obst.* **36**:447-453, 1923. (b) Schoemaker, J.: Zur Technik der Magenresektion nach Billroth I, *Arch. f. klin. Chir.* **121**:268-271, 1922.

recognized that the fatal suture angle could be avoided by improved technic. His contribution was the discovery that by removing all the lesser curvature, and thereby tubing the stomach, secure anastomosis could be made since tension was eliminated, and the size of the end of the stomach was reduced. Likewise W. J. Mayo <sup>2a</sup> showed that ligation of the left gastric artery near its origin added appreciably to the mobility of the stomach. Moreover, Polya <sup>1</sup> in spite of introducing the universally accepted modification of the Billroth II operation (1910), which bears his name, actually favors gastroduodenostomy.

The modern modification of the Billroth I technic as sponsored by Clagett and Waugh,<sup>3</sup> of the Mayo Clinic, and others is not easily applicable to many cases of penetrating heavily scarred duodenal ulcers on account of the difficulties and dangers inherent in mobilizing sufficient of the end of the duodenum to effect direct anastomosis. The situation may be met by utilizing the modification introduced by von Haberer <sup>4</sup> in 1922 and Finney <sup>5</sup> in 1923. Essentially, this consists in closing the end of the duodenum and anastomosing the end of the stomach to the side of the mobilized descending duodenum, terminolateral gastroduodenostomy. Since the von Haberer-Finney modification was presented, numerous references have been made to this procedure in literature, but we have been unable to find any sizable series of case reports.

#### RATIONALE

The following advantages of gastroduodenostomy may be cited:

1. *Anatomic*.—The normal anatomic relationship is restored.
2. *Physiologic*.—Gastric contents after operation are poured into the duodenum, an organ accustomed to receiving acid secretion and, theoretically at least, better adapted for this purpose than the jejunum.
3. *Technical*.—(a) The entire operation is performed in the supracolic compartment, a fact of definite value when dealing with substandard patients and when the procedure must be carried out under local anesthesia, since disturbance of the colon, mesocolon and small intestine is avoided. (b) The duodenal stump should be more secure, since back pressure on this area is impossible. (c) Postoperative gastric retention due to mechanical kinking at the stoma does not occur.

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3. Clagett, O. T., and Waugh, J. M.: Indications for and Advantages of Schoemaker-Billroth I Gastric Resection, *Arch. Surg.* **56**:758-765 (June) 1948. Higginson, J. F., and Clagett, P. T.: The Schoemaker-Billroth I Operation, *Surgery* **24**:613-620, 1948.

4. von Haberer, T.: Terminolaterale Gastroduodenostomie ober der Resektionsmethode nach Billroth I, *Zentralbl. f. Chir.* **49**:1321-1326, 1922.

5. Finney, J. M. T.: A New Method of Gastroduodenostomy, End to Side, with illustrations, *Tr. South. S. A.* **36**:5 and 76, 1924.

The following objections have been raised: 1. The operation technically is more difficult than gastrojejunostomy. 2. Insufficient stomach is resected. This objection is invalidated if the duodenum and stomach are adequately mobilized and the decision to utilize the operation is not made until after the resection is accomplished. 3. Reflux of beneficial alkaline duodenal contents into the stomach is less than after gastrojejunostomy. Continuous postoperative gastric aspiration in comparable groups of patients has shown that there is no appreciable difference in the amount of duodenal contents removed. 4. Complete mobilization of the duodenum increases the tendency to duodenal ileus. This did not occur in any of our patients.

#### PERSONAL EXPERIENCE

An encouraging experience with the von Haberer-Finney gastrectomy in the treatment of jejunal ulcer prompted the use of the technic in gastric ulcer and an occasional early case of gastric carcinoma with gratifying results. Since early in 1946 we have performed subtotal gastrectomy plus vagotomy on practically all patients with duodenal ulcer. This additional procedure appears to be satisfactory, as well as we can judge, for in none of these patients has a jejunal ulcer developed, a statement we could not make regarding any other three year period when subtotal gastrectomy alone was done. Difficulty with gastric retention following vagotomy led us to substitute the duodenum for the jejunum in restoring continuity, and again the result justified continuance of the method. We have now used the operation in 50 cases during 1947 and 1948, but these were not consecutive gastrectomies, since the method is not applicable to all cases. Among the patient's there were 42 with duodenal ulcer, of whom 20 had one or more episodes of hemorrhage, 9 had had perforation and in 25 some degree of obstruction was present. Delayed emptying of the stomach in spite of the concomitant vagotomy was not a problem in any of these patients, and neither the dumping syndrome nor recurrent ulcer has been observed. There was 1 death in the series attributed to hepatic failure on the basis of observations at autopsy, which also showed that the anastomotic suture lines were intact. The closed duodenal stumps and the anastomoses all healed without leakage. Appraisal of end results in the 46 patients who were followed after operation indicated good results in 39 (84.7 per cent) and fair in 7 (15.3 per cent). In other words, the end results were about the same as for a comparable group in which restoration of continuity was established by gastrojejunostomy.

#### OPERATIVE PROCEDURE

1. *Mobilization of the Duodenum.*—The peritoneum and fascia propria lateral to the descending duodenum are sectioned (fig. 1 A), thereby mobilizing both the duodenum and the head of the pancreas

(fig. 1 *B*). This exceedingly useful maneuver<sup>6</sup> not only permits adequate inspection and palpation of these organs to determine the feasibility of resection in penetrating duodenal ulcers complicated by edema and induration but also facilitates closure of the duodenal stump.

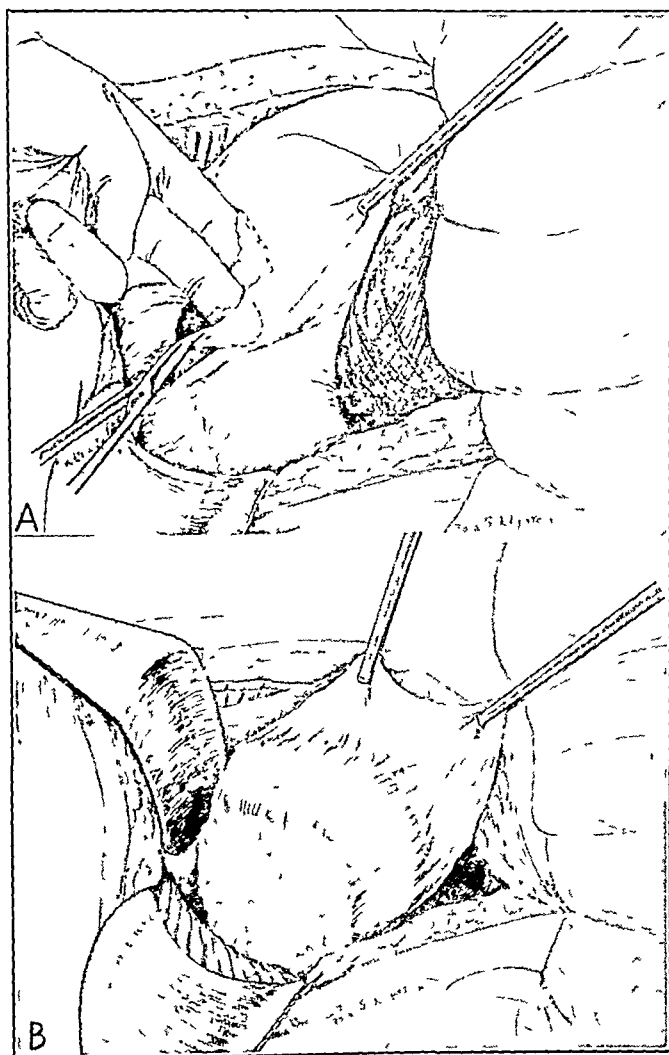


Fig. 1.—*A*, method of mobilizing the duodenum and head of the pancreas. The peritoneum is incised, and then the fascia propria is divided. *B*, completed mobilization of the duodenum and head of the pancreas. This drawing overemphasizes the amount of the peritoneum present.

*2. Ligation of the Left Gastroepiploic Artery.*—The watershed between the right and left gastroepiploic arteries is defined, and the left artery is clamped and tied. Frequently this consists in tying only a

6. (a) Finney, J. M. T., Jr.: Pyloroplasty and Gastroduodenostomy, *Surgery* 2:738-758, 1937. (b) Wilkie, D. P. D.: Some Principles in Abdominal Surgery, *Surg., Gynec. & Obst* 50:129-138, 1930.



slender communicating branch, for in most instances the anastomoses between these two vessels takes place in the gastric wall rather than in the gastrocolic omentum. The last two radicles of the left gastroepiploic artery are then ligated between the greater curvature and the artery to allow a higher removal of stomach.

3. *Ligation of the Right Gastroepiploic Artery.*—This artery is picked up and ligated in the gastrocolic omentum about  $2\frac{1}{2}$  inches (6 cm.) proximal to the pylorus so as not to denude entirely the great omentum of its blood supply. The gastrocolic omentum between the two ligated arteries is cut and tied, as are the primary radicles of the right gastroepiploic artery going to the pylorus and prepyloric region of the stomach. The middle colic artery must be identified and protected during this procedure.

4. *Ligation of the Right Gastric Artery.*—The right gastric artery now is double clamped and ligated (fig. 2), thereby completing mobilization of the pyloric end of the stomach.

5. *Sectioning and Closing the Duodenum.*—A small Payr clamp is put on the stomach just proximal to the pylorus and the duodenum cut across just distal to it. The duodenal stump is closed with a double row of sutures, and the suture line is buried in the head of the pancreas. In difficult cases of penetrating ulcer, it is advisable not to use a clamp on the duodenal side, since every bit of tissue may be needed for the closure.

6. *Ligation of the Left Gastric Vessels.*—The left gastric artery and vein are identified by turning the stomach over to the left and are isolated, clamped, cut and ligated at a point proximal to the first gastric branch (fig. 2). The gastropancreatic omentum is sectioned with the vessels, thereby removing the main support of the stomach<sup>2</sup> and producing maximum mobility of the organ.

7. *Section of the Vagus Nerves.*—Upward retraction of the left lobe of the liver and downward retraction of the mobilized stomach renders taut the triangular peritoneal and fibrous support running from the diaphragm to the esophagus and upper part of the stomach; dividing this structure after clamping and tying, since it contains blood vessels, exposes the esophagus. Continued downward traction on the stomach causes the vagus nerves to stand out like whip cords and renders identification easy. Segments are removed from both nerves for microscopic verification.

8. *Removal of Gastric Segment.*—The completely mobilized stomach is now brought up into the wound, and two parallel  $2\frac{3}{4}$  inch (7 cm.) Kocher clamps (fig. 3) are applied from the greater curvature side at right angles (fig. 4 A) to the long axis of the stomach at a point proximal

to the distal branch of the left gastroepiploic artery. The portion of stomach between the clamps is cut across to a point just beyond their tips, and a pair of  $3\frac{1}{2}$  inch (9 cm.) Kocher clamps are applied at right angles

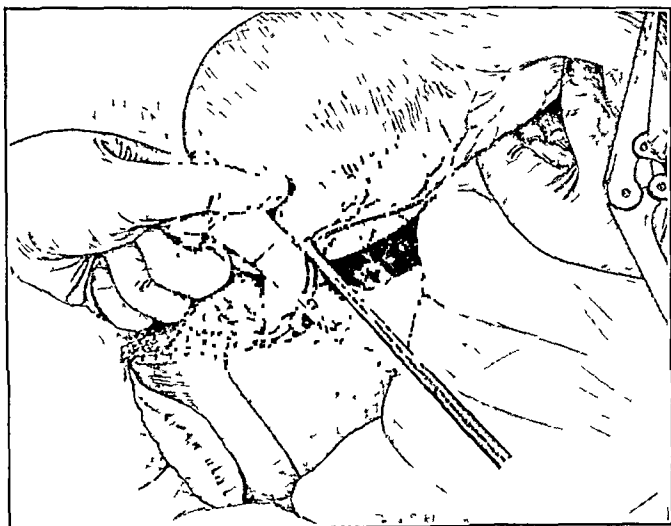


Fig. 2.—Ligation of the left gastric artery. The stomach is turned over to the left. The vessel is clamped, cut and ligated near its origin from the celiac axis. The vagus nerves are sectioned after this step.

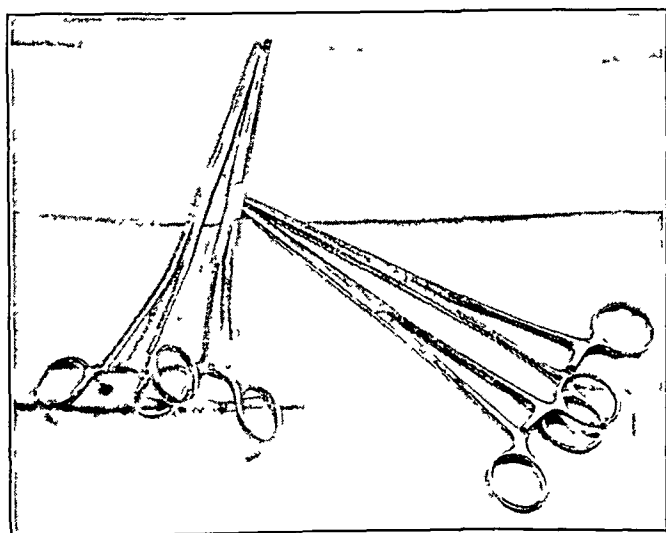


Fig. 3.—Modified Kocher clamps,  $2\frac{3}{4}$  inch clamps used on the side of the greater curvature and  $3\frac{1}{2}$  inch clamps used on the side of the lesser curvature. The handles of the latter are curved to increase ease of application

to the first pair in such a fashion that their distal extremities grasp the lesser curvature just at its junction with the esophagus. Resection is completed by cutting between the clamps (fig. 4 *B*). Inspection of

the removed area reveals that the entire lesser curvature, fully two thirds of the greater curvature and the continuous portion of the body of the stomach have been removed (fig. 5 *A*). This, in effect, achieves what is accomplished by the use of the Schoemaker clamp. We believe that removal of all the lesser curvature is of utmost importance (fig. 4). The upper clamp is now removed, and this portion of the stomach is

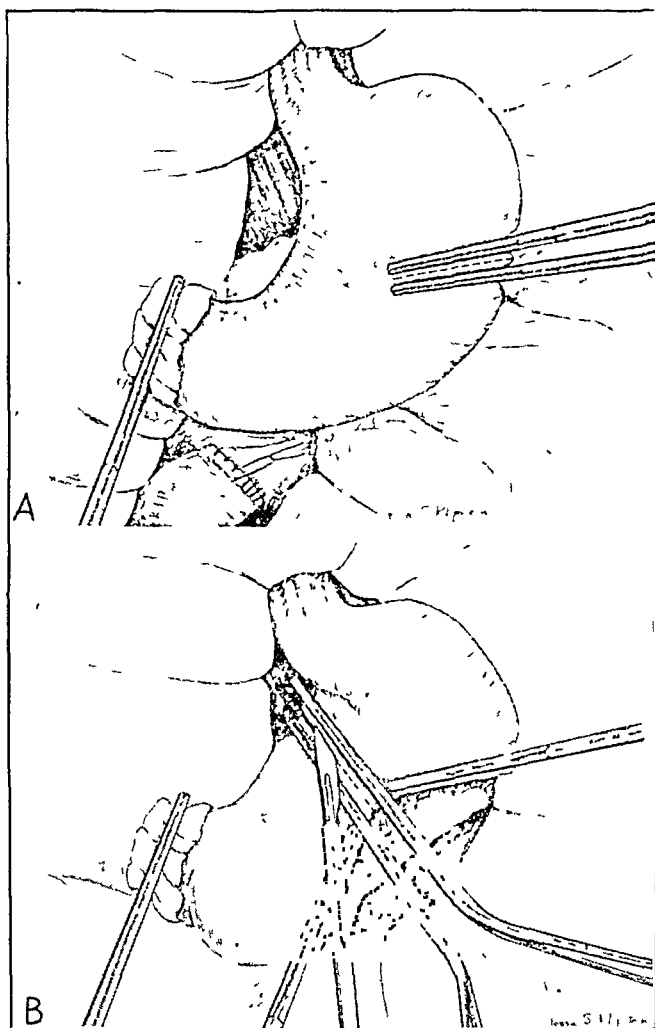


Fig. 4.—*A*, Kocher clamps applied at right angles to the long axis of the stomach at a point proximal to the distal branch of the left gastroepiploic artery. *B*, second pair of Kocher clamps applied at right angles to the first pair in such a fashion that all the lesser curvature will be removed.

closed by a double row of sutures (fig. 5 *B*). It will now be seen that a narrow elongated tube of stomach remains.

9. *Decision as to Type of Restoration of Continuity.*—A trial approximation of the gastric tube to the duodenum is now made (fig. 5 *B*).

If it is obvious that anastomosis can be made without tension, the von Haberer-Finney restoration is proceeded with; otherwise, a retrocolic gastrojejunostomy is carried out. Again we wish to emphasize that the decision regarding the type of anastomosis is not made until this stage of the operation is reached. Usually some additional mobilization of

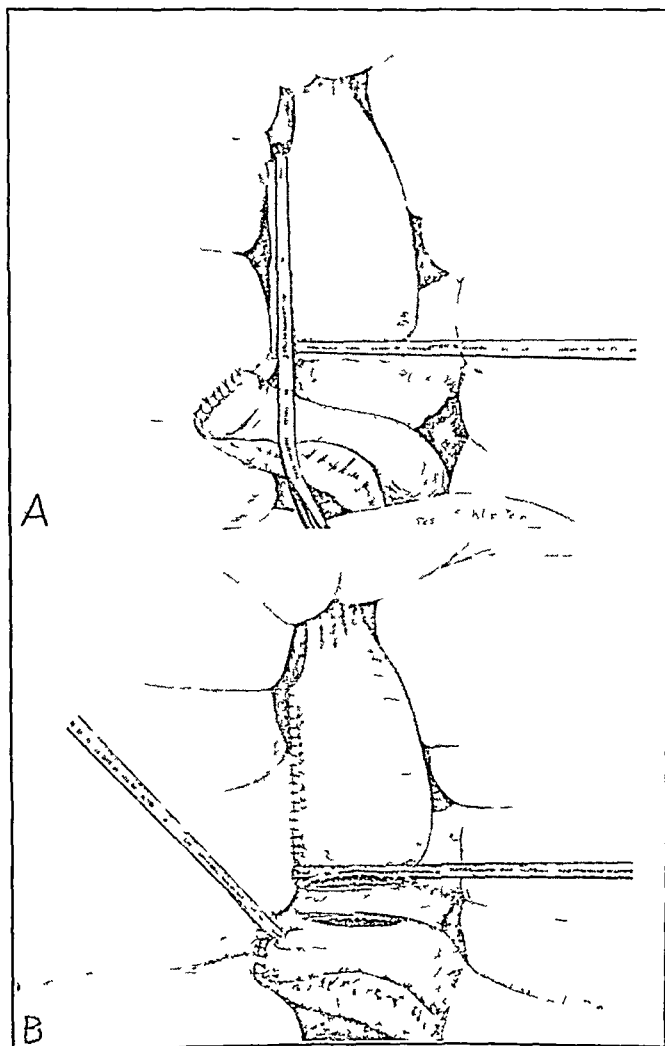


Fig. 5—*A*, stump of stomach remaining *B*, upper clamp removed and this portion of the stomach closed with a double row of sutures. Trial approximation of the gastric tube to the duodenum.

the duodenum and head of the pancreas must be done by further sectioning of the fascia propria. Rarely the hepatic flexure has to be mobilized downward by cutting its outer leaf of peritoneum, but frequently the right margin of the upper leaf of the mesocolon must be brushed downward to expose more of the descending duodenum.

10. *The Anastomosis.*—The posterior wall of the end of the stomach is sutured with interrupted fine silk sutures to the anterior wall of the duodenum close to the mesenteric border of the latter (fig. 6 *A*). A suitable opening is now made in the duodenum, and the anastomosis is completed by a circular interlocking suture of atraumatic surgical gut

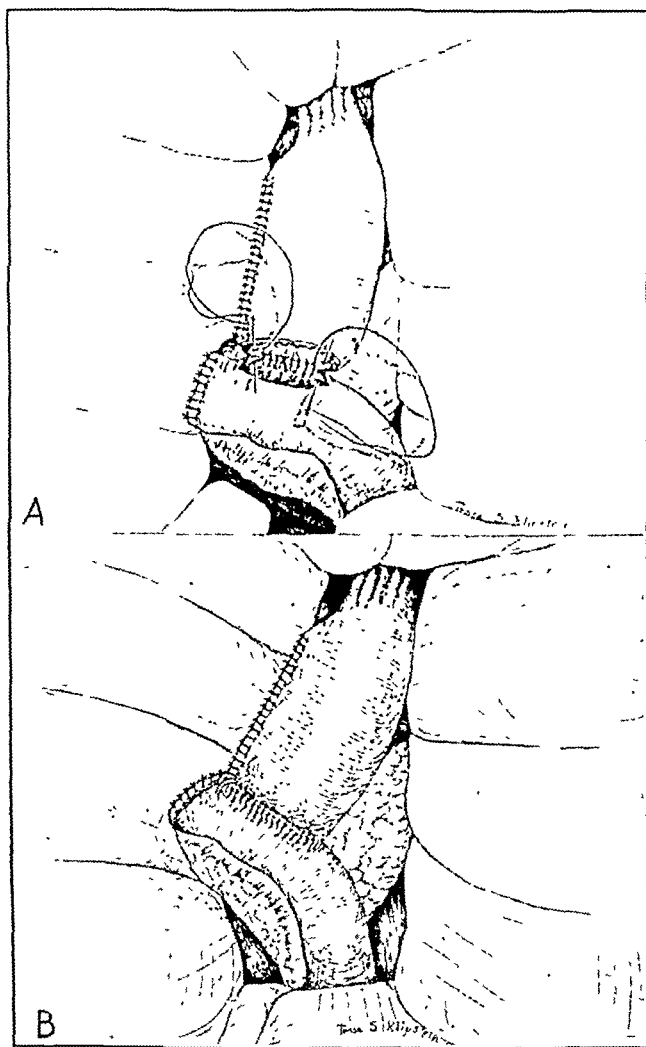


Fig. 6.—*A*, posterior portion of the anastomosis being completed. *B*, completed anastomosis. A purse string suture reinforces the upper angle of the anastomosis.

reinforced anteriorly with interrupted sutures of fine silk (fig. 6 *B*). A precautionary purse string suture draws together the two gastric walls and the duodenum at the dangerous upper three way "angle of sorrows." The anastomosis, which readily admits two fingers, is freely mobile and lies without tension.

## COMMENT

The important features of the operation on which success depends are:

1. Adequate mobilization of the duodenum and the head of the pancreas. This can be effected only by incising the fascia propria or endoabdominal fascia <sup>6b</sup> as well as the peritoneum along the outer border of the duodenum.

2. Tubing of the remaining part of the stomach. High section of the left gastric artery and the gastropancreatic omentum in which it lies produces maximum mobility of the stomach, as pointed out by the late W. J. Mayo.<sup>2</sup> Removal of the entire lesser curvature is a most important step in surgical treatment of peptic ulcer, as emphasized by Schoemaker, Aschoff and the late Roscoe Graham.<sup>7</sup> When these two important steps are completed and the new lesser curvature is reformed, it will be found that the narrow elongated gastric tube which remains can be approximated to the mobilized duodenum without tension.

3. Sectioning of the vagus nerves. This provides an additional 2 inches (5 cm.) in length to the stomach.

4. Making the anastomosis only when maximum mobility has been attained. The slightest degree of tension must be construed as being an absolute contraindication to gastroduodenostomy.

## SUMMARY AND CONCLUSIONS

1. The von Haberer-Finney modification of the Billroth I gastrectomy extends the scope of this sound anatomic and physiologic method of restoring gastrointestinal continuity.

2. Success of the operation depends on adequate mobilization of the duodenum and stomach.

3. Application of the Schoemaker principle of tubing the stomach allows the surgeon to remove as much of the stomach as if restoration were completed by gastrojejunostomy.

4. Although insufficient time has elapsed to allow final conclusions to be drawn, the results so far suggest that the Billroth I principle has much to commend it.

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7. Graham, R. R.: *Technical Surgical Procedures for Gastric and Duodenal Ulcer*, Surg., Gynec. & Obst. **66**:269-287, 1938.

# PRECAUTIONS AND RESULTS IN GASTRECTOMY

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IT IS WELL known that the operative mortality rate following gastrectomy has dropped to one third or one half of the figure encountered fifteen to twenty years ago.<sup>1</sup> The technic of performing gastrectomy and the ability of the surgeon have changed very little indeed during this period. It is obvious, therefore, that a better understanding of the physiology of the gastrointestinal tract with special consideration of preoperative and postoperative care is the major factor responsible for the improvement in the immediate results of gastrectomy. In preparation of this report we have studied material representing 191 gastrectomies for benign and for malignant disease in the Illinois Research Hospital during the past thirteen years. As is usually the case in other reports, our studies on postoperative complications and causes of death have made certain precautions quite obvious, which if utilized might have resulted in a greatly reduced number of complications and deaths. Many of the precautions listed subsequently have been used by us for years; others have only recently been adopted.

## PRECAUTIONS IN PREOPERATIVE CARE

1. For any sick patient a complete examination to determine the presence or absence of complicating diseases is, of course, essential, along with carefully taken history. In patients with gastric lesions, many of whom have obstruction, certain laboratory examinations in addition to routine blood and urine examinations, including determinations of plasma proteins, nonprotein nitrogen and plasma chlorides, are essential in a patient's work-up. It is necessary to accomplish an accurate assay of the patient's physical reserve if operation is contemplated. It is

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1. Bell, H. G.: Problem of Gastric Cancer in a University Hospital, *Surgery* **23**:351, 1948. Walters, W.; Gray, H. K., and Priestley, J. T.: *Carcinoma of the Stomach*, Philadelphia, W. B. Saunders Company, 1942. St. Johns, F. B.; Harvey, H. D.; Ferrer, J. M., and Sengstaker, R. W.: Results Following Subtotal Gastrectomy for Duodenal and Gastric Ulcer, *Ann. Surg.* **128**:1, 1948.

remarkable how accurate an interpretation of the patient's ability to climb stairs and walk certain distances will be in estimating operability.

2. An accurate determination of the degree of obstruction must be made. If there is a history of vomiting or a history of sharp curtailment in caloric intake, obstruction is probably present. It is amazing how commonly a complete obstruction is encountered with only occasional or no vomiting. The most effective method of determining the amount of obstruction is to insert a tube into the stomach through the nasal cavity eight or nine hours after a meal. If the patient has eaten recently and obstruction is fairly complete, an ordinary Levin tube will often become plugged with food particles; accordingly, it is frequently wise to use a large stomach tube for the first examination. Any amount of fluid over 100 cc. represents obstruction. If several hundred cubic centimeters is found, it is usually advisable to maintain decompression with a Levin tube through the nares for two or three days. Frequently, after decompression and consequent relief of edema, the patient will be able to take a fairly large quantity of food by mouth, at least for a few days, thereby improving his malnourished state.

3. Dehydration and hypochloremia must be corrected. If the patient has been taking very little or no fluid by mouth and has been vomiting, both of these conditions will be present. As much as 5,000 cc. of fluid may be necessary during the first twenty-four hours after admission if the patient has obstruction. No more than 10 Gm. of salt should be given per day, even in this early period, until the laboratory values for plasma chloride have been noted. It is not difficult to determine the amount of fluid needed after ten to twelve hours' observation, since the urinary output can then be measured and an estimate made from the amount voided. The urinary output in twenty-four hours should, of course, be 1,000 cc. or better.

4. Anemia must be corrected early. Several transfusions may be needed and should be given in the first two to three days of treatment to bring the patient's hemoglobin level hematocrit value and erythrocyte count to normal.

5. Hypoproteinemia must be corrected. Frequently, administration of enough blood to bring the hematocrit and hemoglobin levels to normal will likewise elevate the blood proteins to a normal or near normal figure. However, if hypoproteinemia exists in spite of adequate blood transfusions, active treatment is indicated, with a high protein diet and plasma and amino acids by the intravenous route; these will be the chief factors in reestablishing body protein.<sup>2</sup> In our hos-

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2. (a) Lyons, C., and Myerson, H. S.: Hemoglobin Deficiency in Protein Depletion, *J. A. M. A.* **135**:9 (Sept. 6) 1947. (b) Clark, J. H.; Lyons, C., and others: Concept of Chronic Shock, *Ann. Surg.* **125**:638, 1947. (c) Varco, R. L.: Nutritional Preparation for Substandard Risk Patients, *Surg., Gynec. & Obst.* **84**:611, 1947.



pital, which takes care only of charity patients, the percentage of patients with at least some degree of obstruction accompanying their gastric lesions was as high as 30 to 40 per cent. Practically all of them manifest a hypoproteinemia along with a loss of weight varying from 10 to 30 pounds (4.5 to 13.5 Kg.) within the previous few months. Correction of this malnutrition is entirely essential before an operation can be considered.<sup>2a,b</sup> By obtaining an early estimate as to the amount of obstruction, we can obtain maximum caloric intake by giving the patient a liquid and soft diet containing 500 to 1,500 calories, supplementing it with plasma and amino acids intravenously. If the patient is able to take as much as 500 calories by mouth in twenty-four hours, his condition can invariably be improved by meticulous preoperative care over a period of several days. However, if the patient has sufficient obstruction to prevent any oral intake, it will be very difficult to improve his nutrition by intravenous therapy although dehydration and hypochloremia can obviously be corrected. The condition of the patient, including weight, etc., will be the factor determining how long the patient should be treated preoperatively with intravenous therapy (in the absence of oral intake) before resort to operation. If we do not have evidence of improvement in the patient's condition in three to four days, we submit the patient to operation at this time if obstruction at the pylorus is complete. Obviously a true subtotal gastrectomy in such circumstances will be associated with a high mortality rate.

6. Vitamin therapy is important when the patient shows evidence of malnutrition with decrease in oral intake from day to day. If the patient is able to take small quantities of food by mouth, the vitamins may be given orally; otherwise they will have to be given intravenously. In view of the severe deficit associated with semistarvation, more than the daily requirements will have to be given. For example, daily dosage equal to 20 mg. of thiamine hydrochloride, 5 to 10 mg. of riboflavin, 200 mg. of nicotinic acid and 200 to 400 mg. of ascorbic acid is indicated.

#### IMPORTANT POINTS IN OPERATIVE TECHNIC

Although the type of operation will be determined to some extent by the nature of the lesion, whether benign or malignant, high resection is indicated in either case, even though the lesion may be located in the pylorus. We prefer the posterior Polya operation but utilize an anterior Polya and a Hofmeister Polya operation on certain occasions.

Regardless of the type of operation performed, Wangenstein<sup>3</sup> has shown that a relatively short afferent loop of jejunum should be

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3. Wangenstein, O. H.: Importance of Short Afferent Duodenojejunal Loop in Gastric Resection for Ulcer, *Bull. Minnesota M. Foundation* 4:82, 1944.

left between the ligament of Treitz and the lesser curvature of the stomach. However, we have not been particularly alarmed about an extra inch or two (2.5 or 5 cm.) of jejunum because we have not seen any marginal ulcers in the patients on whom we have performed an anterior Balfour-Polya operation, which of necessity leaves a longer afferent loop than does a posterior Polya operation. The only 2 marginal ulcers which we encountered in our patients on whom gastrectomy had been done at our hospital occurred in patients who had had a posterior Polya operation.

When a posterior operation is performed, it is essential that the edges of the mesocolon be anchored to the stump of stomach to prevent herniation with consequent intestinal obstruction. When the resection has been unusually high, great care must be exercised lest a kink be produced where the afferent loop joins the lesser curvature of the stomach. Since an obstruction at this point would be very dangerous from the standpoint of "blow-out" of the duodenal stump, it is commonly desirable in high resections to do a Hofmeister type of operation, turning in the medial half of the stomach and leaving the opening in the outer half adjacent to the greater curvature for anastomosis to the jejunum.

We have become convinced during our experience of the past few years that a duodenal ulcer should not be resected if its removal would leave such a short stump as to jeopardize its inversion. We have left 37 duodenal ulcers *in situ* and have had no complications arising therefrom. The only exceptions to this attitude in therapy, which is held by most surgeons, is in patients with active hemorrhage.

Not infrequently it will be very difficult or impossible to have a satisfactory inversion of the stump of the duodenum because of induration of the walls secondary to the ulcer and consequent inflammation. Occasionally sufficient duodenum may be freed from the inflammation involving the pancreas by inserting the index finger of the left hand into the duodenum while the dissection is being made. In instances in which even this is impractical, we resort to a procedure practiced by many in which we leave about 2 cm. of pylorus attached to the duodenum but are careful to excise all the mucous membrane.<sup>4</sup> This portion of the pylorus usually allows a sufficient turn-in, but if it is still difficult to obtain good inversion of the stump the two walls of the pylorus can be approximated with two rows of interrupted fine silk placed from the inside, but superficially to preserve all the blood supply possible. When this procedure is done, it is safer to add a third reenforcing layer by closing the end of the stump with a continuous

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4. Schilling, J. A., and Pearse, H. E.: Re-Evaluation of Role of Pyloric Antrum in Marginal Peptic Ulcers, *Surg., Gynec. & Obst.* **87**:225, 1948.

0000 chromic surgical gut suture and cover the stump with omentum. Such a closure may be life saving in certain cases when induration of the duodenum makes inversion impossible or extremely dangerous. However, we wish to emphasize that closure by approximation is not as safe as inversion, although we have not had a duodenal leak with any stumps closed by the approximation technic.

Before the last few sutures in the anastomosis are taken we reach in with long forceps and thread the end of the Abbott-Rawson tube down through the efferent loop of jejunum. This allows us to feed the patient immediately and yet decompress the stomach.

It is not within the scope of this paper to discuss in detail the indications for vagus section. However, we can summarize our use of this operation by stating that we use it in all patients with marginal ulcers and in many elderly patients who are poor risks, particularly if obstruction is present. When it is performed, a gastroenterostomy should also be done, regardless as to whether or not obstruction is present, because vagus section is so commonly followed by pyloric spasm for a variable length of time. It is agreed by all that vagus section is not effective in gastric ulcer. Likewise, most surgeons agree that vagus section is very effective in the treatment of a marginal ulcer.

#### PRECAUTIONS IN POSTOPERATIVE CARE

1. Ample amounts of fluid are given to maintain urinary output of 1,000 cc. per day; it is true, however, that what appears to be adequate fluid intake for the twenty-four hour period immediately following operation rarely results in an output of 1,000 cc. There is an obvious oliguria for several hours following operation. In general, the amount of fluid per day should be equal to 2,500 cc. plus the amount obtained by decompression. We utilize 5 per cent dextrose and amino acids to a great extent.

2. The salt intake must be limited sharply during the immediate forty-eight hour period following operation.<sup>5</sup> We give no salt during this time except that which is contained in the amino acid solution. After the first forty-eight hour period little or no salt will be needed by vein, since in ordinary circumstances we are feeding the patient a liquid diet through the Abbott-Rawson tube; accordingly, he should be getting enough salt in his food unless he is draining unusually large quantities from the stomach.

3. The patient must be turned frequently and encouraged to cough as soon as he comes out of the anesthesia. We ambulate these patients the day following operation and daily thereafter except those who are

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5. Coller, F. A.; Campbell, K. N.; Vaughn, H. H.; Iob, L. V., and Mayer, C. A.: Postoperative Salt Intolerance, *Ann. Surg.* **119**:533, 1943.

extremely weak because of malnutrition or other cause. If signs of atelectasis develop or if secretions are rather profuse, the patient will usually not be able to cough out the material himself. In such circumstances it will be necessary to insert a catheter through the nose and guide it into the trachea after the pharynx is sprayed with cocaine.<sup>6</sup> If this type of aspiration does not clear the mucus from the bronchi and if there is still residual evidence of atelectasis, there should be no hesitation in performing bronchoscopy with direct aspiration of the main bronchial stumps.<sup>6</sup>

4. To encourage deep breathing and minimize atelectasis, inhalations of carbon dioxide should be given every hour for the first few days except while the patient is asleep.

5. The Abbott-Rawson tube is removed on the third to the fifth day but only after it has been shown that the stoma is open. A fairly accurate estimation as to the function of the stoma can be determined by clamping the tube overnight and applying suction the next morning to determine how much fluid is retained in the stomach. This test is probably of more value if the patient is given 200 to 300 cc. of water to drink in the evening before the tube is clamped off. Although some patients are disturbed considerably by the presence of the Abbott-Rawson tube, the majority of them do not complain about it, and we therefore do not hesitate to leave it in place for five days, particularly since maintenance of daily caloric intake is important in most of our patients, who are so malnourished at the time of admission to the hospital.

#### ANALYSIS OF CASES

The material utilized as a basis for this report includes the cases of 191 patients in whom gastrectomy was performed at the Illinois Research Hospital during the thirteen year period from January 1936 to January 1949, inclusive.

These cases are presented according to diagnosis in table 1. Of the 191 operations performed, 114 were for benign and 77 were for malignant lesions. The gastric and duodenal ulcers were almost evenly divided, while in 11 cases both gastric and duodenal ulcers were demonstrated. There were 7 instances of marginal ulceration which had appeared after previous gastrectomy. Only 2 of these were in patients previously operated on at our hospital.

There were 75 gastrectomies for carcinoma. Forty-eight, or almost two thirds of these patients, had demonstrable metastases, and a few of these had purely palliative operations.

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6. Haight, C.: Intratracheal Suction in the Management of Postoperative Pulmonary Complications, *Surgery* 6:445, 1939.

The types of operation utilized and the operative deaths associated with each are shown in table 2. There were 14 deaths in 184 subtotal resections, whereas in 7 total resections there was 1 death. The anastomosis was placed in a retrocolic position in 114 of the cases; in 60 it was found advisable to place the anastomosis anterior to the colon. In 7 instances resection of a gastroenterostomy stoma in addition to a subtotal gastrectomy was made necessary by the presence of marginal ulcers. In only 2 of these had the initial gastrectomy been performed in this hospital. Of the 7 marginal ulcers, 2 were further complicated by the presence of gastrojejunal fistulas. In these 2 cases the

TABLE 1.—*Summary of Partial and Complete Gastrectomies, Illinois Research Hospitals, January 1936 to January 1949*

Diagnosis	No. of Cases <sup>a</sup>
Ulcer.....	114
Gastric.....	45
Duodenal.....	51
Gastric and duodenal.....	11
Marginal.....	7
Carcinoma.....	75
Regional metastases.....	48
Lymphosarcoma.....	1
Reticulum cell sarcoma.....	1
Total.....	191

TABLE 2.—*Type of Operation*<sup>§</sup>

		Number	Deaths
Subtotal gastrectomy.....		184*	14
Polya.....	174		
Resection of gastroenterostomy stoma.....	7	...	0
Hofmeister.....	3	...	0
Total gastrectomy.....		7	1
Total.....		191	15

\* Resections of the cardia and terminal end of the esophagus are not included.

patients were similarly treated by resection of the stomach and the involved portion of the colon after preliminary colostomy.

The postoperative period was without complication in 123 cases in this series. There were a total of 88 complications which presented themselves in the remaining 68 patients. These complications and their incidence are presented in table 3. An analysis of these complications revealed that the deaths were centered for the most part in a relatively few of the complications. Therefore, we present in table 4 the complications which made specific contributions to the mortality herein reported.

Cardiac complications were responsible for 3, or 20 per cent, of these deaths and pulmonary complications in the form of atelectasis, pneu-

monia and pulmonary embolism contributed another 20 per cent of these deaths. This leaves 60 per cent of our mortality rate that resulted from complications which we consider preventible. Wound disruption occurred in 4 per cent of this series and was responsible for 1 death. There was 1 death from massive hemorrhage in a bleed-

TABLE 3.—*Complications Following 191 Gastrectomies*

	Number	Deaths
Atelectasis.....	19	1
Pneumonia.....	13	2
Wound infection.....	11	0
Wound disruption.....	9	..
Peritonitis.....	7	..
Obstruction.....	7	..
Stomal.....	5	..
Intestinal.....	2	..
Perforated duodenal stump.....	4	3
Peritoneal abscess.....	3	0
Diarrhea.....	3	0
Pulmonary abscess.....	3	..
Acute heart failure.....	3	3
Pulmonary embolus.....	2	1
Perforation of jejunum.....	2	2
Urosepsis.....	1	1
Massive hemorrhage.....	1	1
	<u>88</u>	<u>15</u>

TABLE 4.—*Mortality Rate for Gastrectomies*

	Cases, Number	Mortality, Percentage
Subtotal gastrectomy.....	184	7.6
Carcinoma and sarcoma.....	70	11.4
Ulcer.....	114	5.2
Gastric.....	45 (6.6)*	
Duodenal.....	51 (5.8)	
Gastric and duodenal.....	11	
Marginal.....	7	
Total gastrectomy		
Carcinoma.....	7	14.2

\* Figures in parentheses represent percentages.

ing duodenal ulcer. There were 2 deaths from jejunal perforations. One was the result of a jejunal ulcer adjacent to the anastomosis; the other was a perforation of a small hemorrhagic spot on the jejunum just distal to an esophagojejunostomy. It will be noted that post-operatively obstruction occurred in 7 cases; in 5 of these the site of obstruction was the stoma. There were 2 instances of obstruction of

the efferent jejunal limb. One of these was a result of simple kinking and was relieved by operation; the other was a result of torsion of the jejunal loop which encouraged the efferent limb to migrate posteriorly and to the right of the afferent limb. The result was gangrene and death. The most dangerous complication encountered was leakage of the duodenal stump, which occurred in 4 cases. In 1 of these the cause of death was determined at necropsy to have been atelectasis, the leaking stump being only an incidental finding. The deaths of the other 3 patients were charged directly to the leak in the duodenal stump.

The mortality figures are presented in table 4. In 184 subtotal gastrectomies there were 14 deaths, constituting a mortality rate of 7.6 per cent. Eight of the patients who died had carcinoma or sarcoma, giving a mortality rate for malignant lesions of 11.4 per cent. The remaining 6 deaths were of patients operated on for complications of ulcers, with a resultant mortality rate of 5.2 per cent for benign lesions. There were 3 deaths each of patients operated on for duodenal and for gastric ulcers, with the mortality rates for the two groups of lesions being slightly higher in the latter group. There was 1 death among 7 patients subjected to total gastrectomy, or a mortality rate of 14.2 per cent.

#### COMMENT

The steadily improving mortality rate associated with gastrectomy has been quite generally observed. Credit for this encouraging trend doubtless lies in many factors, including improvements in methods of anesthesiology, the advent of the antibiotics and chemotherapeutic agents, increasing familiarity of surgeons with the procedure and, as previously mentioned, a better understanding of the physiology of the gastrointestinal tract. We feel that the emphasis on physiology as it is related specifically to the preparation and postoperative care of these patients is the most important single factor in the progressive improvement in results from this operation.

The patient who presents himself with a gastric or duodenal lesion today, even without obvious obstruction, is recognized to be nutritionally depleted until proved otherwise. With the laboratory reports properly evaluated in the light of the usual study of loss of weight, we deny or confirm the existence of that state of nutritional depletion which Lyons and Mayerson<sup>2a</sup> have termed "chronic shock." These workers, as have Varco<sup>2b</sup> and others, emphasized the importance as well as the methods of correcting these nutritional deficiencies prior to operation. The recognition that these poor risk patients, once their nutritional equilibrium has been restored, may become fair or even good risks has contributed to the broadening scope of the indications for gastrectomy.

We were particularly interested in the complications contributing to mortality as presented in table 5.

The cardiac and pulmonary complications together represented 40 per cent of the mortality reported. The deaths from cardiac complications occurred in patients whose cardiac status had been evaluated by medical consultants who assisted in their preparation for operation. We are inclined to classify them as unavoidable. The pulmonary complications were responsible for 3 or 20 per cent of the deaths, but it is to be noted that the incidence of these pulmonary complications, including atelectasis, pneumonia and pulmonary embolus, totals 34, or 55 per cent, of these potentially fatal complications. We therefore feel that we have kept fatalities from pulmonary complications near the minimum. There remains for consideration 60 per cent of the operative mortality here reported. Eight of these 9 deaths we feel may be classed as avoidable.

TABLE 5.—*Complications Contributing to Mortality*

	Incidence	Deaths
Atelectasis .....	19	1
Pneumonia .....	13	1
Wound disruption .....	9	1
Obstruction .....	7	1
Duodenal stump leak.....	4	3
Acute heart failure.....	3	3
Pulmonary embolus .....	2	1
Perforation of jejunum.....	2	2
Massive hemorrhage .....	1	1
Urosepsis .....	1	1
Total .....		15

The leaking duodenal stump has been recognized as the complication most to be feared in gastrectomy. In general, its incidence is greater in gastrectomy for duodenal ulcer than in gastrectomy for gastric ulcer, because the presence of the ulcer in the duodenum will interfere with inversion of the duodenal stump. This relatively greater incidence of leakage of the stump following gastrectomy for duodenal ulcer usually results in a higher mortality rate than in gastrectomy for gastric ulcer. However, in our series, the mortality was approximately the same in the two groups, perhaps because we have been exceedingly careful in closure of the stump when the gastrectomy was performed for duodenal ulcer.

The death from massive hemorrhage occurred in a duodenal ulcer previous to the formation of our present policy, which calls for surgical intervention in bleeding ulcers which fail to maintain circulatory stability once it has been established or in those who present a history of more than two severe incidents of bleeding.

There were 2 jejunal perforations, 1 of which was in a marginal ulcer. The more generous resections routinely accomplished today



tend to decrease the incidence of the gastrojejunal ulcers and consequently, of the complications that may arise therefrom. The other jejunal perforation was through a small hemorrhagic spot near an esophagojejunal anastomosis, most likely the result of inadvertent trauma.

The 7 patients with postoperative obstruction included 5 in whom the site of obstruction was the stoma. Of these, 4 were relieved by conservative measures and 1 required reoperation. None died. There were 2 patients with obstruction of the efferent jejunal limb. One of these had simple kinking which was relieved by operation. In the other the obstruction was the result of torsion of the jejunal loop with resultant gangrene and death. The latter 2 cases emphasize the point made by Mayo<sup>7</sup> of the importance of the proper placement of the efferent jejunal loop so that it descends from the gastrojejunostomy into the left abdominal fossa posterior to the remaining part of the small bowel.

#### SUMMARY

Progress made in the knowledge of physiology during the past twenty-five years resulting in improved preoperative and postoperative care has unquestionably been a much more important factor in lowering mortality rate during this period than has improvement in surgical technic. Important precautions in minimizing the mortality rate following gastrectomy are correction of dehydration, electrolytic imbalance, anemia and hypoproteinemia before operation is performed. In our estimation the use of the Abbott-Rawson tube has been of definite value in postoperative care in our patients. Likewise, in our estimation, limitation of the salt intake to no more than 1 or 2 Gm. during the first two days postoperatively has been an important factor in eliminating postoperative oliguria.

This study includes a survey of 191 gastrectomies performed at Illinois Research Hospital during the past thirteen years. The mortality rate was 11.4 per cent for subtotal gastrectomy for carcinoma and 5.2 per cent for ulcer, or an average of 7.6 per cent for the series of 184 subtotal gastrectomies. During the past few years the mortality has obviously been lower than during the first part of the period studied. It is anticipated and expected that the rate in gastrectomy for benign ulcer at the present time should be less than 3 per cent.

Atelectasis was the commonest complication but accounted for only 1 death. Pneumonia was diagnosed in 12 cases, but only 1 of these patients died. The highest number of deaths from any single complication occurred in leakage of the duodenal stump (13 deaths) and cardiac disease (3 deaths).

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7. Mayo, W. J.: Technic of Gastrojejunostomy, *Ann. Surg.* **43**:539, 1906.

## DISCUSSION OF PRECEDING PAPERS

DR. JAMES T. PRIESTLEY, Rochester, Minn.: The very careful studies of Drs. LaBree and Gillespie are illuminating. I think that one of the points which Dr. LaBree made is worth while emphasizing—namely, the importance of the amount of stomach resected in the treatment of duodenal ulcer. It is very difficult to evaluate results of partial gastrectomy for duodenal ulcer which are reported in the literature if the amount of the stomach resected is unknown. Obviously, the physiologic basis for the operation is the reduction of gastric acidity, and the results will vary depending on the amount of the stomach removed. The type of anastomosis performed would seem to be of secondary importance.

I do not know that it has ever been shown that it makes a tremendous difference how much of the stomach is resected so far as the "dumping syndrome" is concerned. Possibly it does make a difference, but it has been my impression that in this particular regard the type of anastomosis is a factor of importance.

Regarding Dr. Fallis' paper, I certainly agree that the Billroth no. 1 operation has many features which appeal from the physiologic point of view. With this operation normal anatomic relationships are more closely preserved, which always seems desirable, and, secondly, it is a simpler procedure technically than an anastomosis of the remaining portion of the stomach to the jejunum. On the other hand, it should be emphasized, as Dr. Fallis mentioned, that this operation should not be decided on until an adequate amount of the stomach has been removed and should not be performed if there is any tension at all on the suture line, as in those circumstances difficulties may follow.

I wondered why Dr. Fallis seemed to prefer the von Haberer type of Billroth no. 1 operation, as it seems to me that this requires more in the way of duodenal mobilization and suture lines than the Shoemaker type, which was illustrated in his figure 5, in which the lower end of the stomach is anastomosed directly to the end of the duodenum.

Regarding Dr. Eastman's paper, I should like to ask him a question concerning postoperative complications in the small group of cases in which the exclusion type of resection was performed after removal of mucosa in the remaining pyloric antrum. It has been my feeling in doing this type of operation, although I do not do it often, that I never can be quite satisfied with the closure of the stump, and in circumstances in which resection, severing the gastrointestinal tract through the duodenum, is not feasible, I have thought that it might be better to do some other type of operation rather than to take a chance with the stump.

As emphasized by Dr. Eastman, I think that we have been remiss in the past in providing an adequate caloric intake for the patient during the first week or so after gastric resection. Even though tube feeding is employed, total caloric intake during this period may be less than one would desire unless a careful check is made of the actual nutritive value of the food supplied. On the other hand, many patients after gastric resection do not require an indwelling tube. They are able to take food by mouth very early during the postoperative period, and the surgeon should be certain in these circumstances that sufficient calories are provided to meet the metabolic needs of the patient. Several years ago my colleagues and I discovered that the diet which we employed after operations on the stomach did not fulfil the daily needs of the patient until almost a week after operation, which obviously is undesirable. There is, of course, no

doubt that adequate nutrition is a factor of great importance during any post-operative convalescence.

DR. WARREN H. COLE, Chicago: In the discussion of gastrectomy, I should like to emphasize the great value of the Abbott-Rawson tube, since it allows one to start feeding the patient even the same day as the operation and yet maintain continuous decompression of the stomach. Nutrition is particularly important in our patients, since all are of the charity type and many are malnourished when first seen.

Regarding perforations of the duodenal stump after gastrectomy, we have had too many of those. They are usually commonest in gastrectomy for duodenal ulcer, because the ulcer complicates inversion of the stump, but in our series the incidence was just as high in gastrectomy for carcinoma.

Our experience, though small, might suggest that obstruction caused by a kink of the proximal arm of jejunum at its point of anastomosis to the lesser curvature is probably a greater cause of "blow-out" than anything else. Accordingly, one should always inspect this area at the termination of the operation but preferably should try to estimate before starting the anastomosis whether or not kinking may occur.

In general, an obstruction at this point would be most likely to occur in extremely high resections, and in such cases the Hofmeister procedure will shorten the proximal loop of jejunum and thus minimize the danger of obstruction.

Dr. Eastman remarked that we had 2 marginal ulcers in our series of gastrectomies. Both occurred in the posterior Polya operation. We had none in our anterior Polya operations.

I think that brings up an important point because some people have been talking about the necessity of having a very short proximal loop of jejunum and about the danger of doing the anterior operation. Since we did not have any in our anterior Polya resections, I am not so inclined to worry about the danger of doing anastomoses anterior to the colon if I think there is indication.

Not long ago it was considered necessary to excise the ulcer when doing a resection of an ulcer. However, of late years most surgeons leave the ulcer in place if it appears that resection would be dangerous. By leaving the ulcer when its resection might be difficult or would jeopardize closure of the stump, I am sure that we are lowering our mortality rate and not increasing the difficulties postoperatively. At any rate, we have no postoperative symptoms or other difficulties which might have been explained by failure to remove the ulcer.

We have had 3 or 4 cases which might be classified as instances of the dumping syndrome, but they were very inconsistent, and I am not sure that we had more than 1 true case of dumping syndrome. None of these occurred in the Hofmeister operation.

I wish to emphasize that the mortality rate of gastrectomy has decreased even during the past five years. Our over-all mortality rate for benign lesions during the twelve year period was a little over 5 per cent. However, of recent years it is less.

I feel sure that at the present time almost all important surgical groups are operating on benign lesions with a mortality rate of under 3 per cent. The mortality rate in gastrectomy for carcinoma will be twice that for benign lesions.

DR. HENRY K. RANSOM, Ann Arbor, Mich.: In general, my experience with gastrectomy has been similar to that which was reported by the essayists. In the past, the duodenal exclusion operations of Devine and Finsterer have been employed

for certain duodenal ulcers in which resection by the conventional method would have entailed difficulty in obtaining a satisfactory closure of the duodenal stump. The results have been far from satisfactory.

Thus, in 14 cases of simple transection of the stomach through or above the antrum and reconstruction by an end to end gastrojejunostomy (Devine), follow-up studies showed that only 2 patients were well, 3 were improved and in 9 the results were poor.

In 22 patients treated by Finsterer's resection for exclusion, 7 were well, 5 were improved and 10 had poor results. When the Finsterer procedure was modified by exenteration of the mucosa of the antral segment in 29 cases the results were: well, 25; improved, 1, and poor, 3. For the present I have discontinued the use of vagotomy in order to evaluate more fully the results thus far obtained. An interim evaluation of 57 cases of gastroduodenal ulcer treated by vagotomy alone or in conjunction with some other procedure (excluding resection) shows the results to be good in 35, or 61.4 per cent; fair in 16, or 28.1 per cent, and poor in 6, or 10.5 per cent.

DR. M. G. GILLESPIE, Duluth, Minn.: As co-author of the paper read by Dr. LaBree, I might just say that we have felt, so far as vagotomy or vagotomy and gastroenterostomy is concerned, that there are others in a better position than we to judge this procedure. Secondly, we have felt that not enough time has elapsed to judge properly the question of vagotomy or vagotomy and gastroenterostomy. The third reason that we continue and will continue to perform what we consider adequate partial gastrectomy is that, although we know that it is not an ideal operation, for the patient with chronic complicated duodenal ulcer it offers a gratifying result in a high percentage of cases.

DR. LAURENCE S. FALLIS, Detroit: In reply to Dr. Priestley's question as to why the von Haberer-Finney modification was used instead of the Billroth no. 1 operation, the point I wish to make is that one can extend the scope of the Billroth no. 1 technic by using this modification. In many cases of penetrating duodenal ulcers it is often difficult and sometimes impossible, at least for me, to make a satisfactory end to end anastomosis. I have, therefore, chosen this method because of its safety factor.

I agree with Dr. Cole that the most important item in duodenal blow-out is the prevention of back pressure, and it is just in this type of patient, in which one feels insecurity of closure of the duodenum, that the von Haberer-Finney lateral anastomosis will add the safety factor, since it eliminates back pressure on the duodenal stump.

It seems to me that one point in the technic of closing the duodenal stump that has not been emphasized enough is mobilization of this organ. I am accustomed to telling my residents that I have learned much of my surgery backward, that I had never learned how to take care of a difficult appendectomy until I resected a few right colons and, by the same line of reasoning, it was not until I had had the opportunity of mobilizing the head of the pancreas and the duodenum in the Whipple operation that I observed and recognized the value of this maneuver in resecting difficult duodenal ulcers. It is a much simpler matter to close the duodenal stump when the duodenum and head of the pancreas have been completely mobilized than when one has to do it in the depth of the wound.

Another item of importance in the security of closure is the importance of not separating the duodenum from the head of the pancreas too much. In other

words, some of the blow-outs are due to necrosis of the duodenal wall resulting from damage to blood vessels which inevitably follows undue mobilization of the duodenum from the head of the pancreas.

DR. WARD H. EASTMAN, Chicago: In answer to Dr. Priestley's question, first, we prefer to turn in a duodenal stump whenever it is possible. When it is not possible, we prefer to turn in an antral stump, but we recognize a certain condition in which the thickness of the antral wall makes it dangerous to try to accomplish a turn of the antral stump, and it is in those instances that we turn to closure by approximation of the antral stump. We have 1 case in which a thick antral stump was turned in, and in retrospect we feel that if this case had been dealt with by approximation of the antrum we might have avoided this fatality. There have been no deaths in those instances in which we have found it advisable to close by approximation.

## BLOOD TRANSFUSION AND REACTION IN SURGICAL PATIENTS

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**P**ERHAPS there is no more important consideration when a transfusion of blood is requested than to remember the possibility of a complication during or after transfusion. For instance, the benefit to be gained from the transfused blood might not be important enough to the patient's progress to justify taking the chance of a possible untoward reaction. Nearly thirty years ago Pemberton<sup>1</sup> expressed the opinion that "the procedure is very often considered only a simple intravenous medication or a minor operation while in reality its potential dangers place it with major operations."

Possibly realistic views such as this one have been insufficiently appreciated, for it is known that even today a number of untoward reactions and occasional fatalities occur in a certain percentage of all instances in which blood is transfused.

In the last few years, and particularly during World War II, the thought, study and research expended on this subject exemplify the importance that is now being placed on the value of the transfusion of blood.

The inestimable benefits of, and the spectacular results obtained from, the administration of blood and plasma during the recent war constitute a subject apart from this paper. The great advances of the last ten years in knowledge about the use of this therapeutic procedure are by this time well known to almost everyone.

In fact, the average person today is more than mildly interested in the use of blood, plasma and other similar agents. The extensive work of the Red Cross in this field during the war did much to familiarize the public with the value of blood and how it is collected, stored and dispensed to the sick and injured. Many persons are superficially

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From the Section on Anesthesiology, Mayo Clinic.

Read at the Sixth Annual Meeting of the Central Surgical Association, Cleveland, Feb. 19, 1949.

1. Pemberton, J. deJ.: Practical Considerations of the Dangers Associated With Blood Transfusions, J. Iowa M. Soc. **10**:170-173 (June) 1920.

familiar with such things as blood groups, the Rh factor and the possibility of untoward reactions.

Because of the marked interest in the subject now manifested by members of the public and because we physicians owe everyone the best treatment that can be evolved, it behooves all physicians to be as familiar as possible with the indications for and contraindications to the transfusion of blood. Moreover, when this method of treatment is actually employed, the ever present possibility of the occurrence of an untoward reaction during or after transfusion must be constantly in mind. These untoward reactions have occurred and will continue to occur, even in the hands of the most skilled medical personnel and in the most meticulously supervised transfusion service. This fact must be accepted. However, to minimize the effects of these almost inevitable occasional reactions, we should be able to recognize the signs and symptoms which they produce, and we should know how to treat them.

Some physicians are under the impression that transfusion reactions will not occur if a patient is under the influence of an anesthetic agent. This idea we hope to dispel, because the truth is that all types of transfusion reactions do occur to patients during surgical procedures. Perhaps this wrong impression has arisen from the fact that transfusion reactions do occur among anesthetized patients, but the signs and symptoms frequently are masked by the action of the anesthesia, so that the reactions go unrecognized.

We shall not go into the details of such laboratory procedures as the determination of blood groups and Rh factors or the reading of cross matching tests that are important parts of a successful transfusion service. It may be said in passing that because of the absolute necessity of accuracy in the performance of laboratory procedures and the always present danger of human error, the laboratory plays a formidable role in a successful transfusion of blood. Every physician, of course, seeks to administer compatible blood, group for group, or low-titered group O blood to patients whose blood group is AB, A or B and to administer Rh-negative or Rh-positive blood as may be indicated.

Correct withdrawal and storage of blood from physically fit donors are essential. The administration of compatible blood is essential. Cross matching of donor's and recipient's blood is desirable. However, in dire emergencies it is our practice to administer blood without cross matching if time does not permit this procedure.

Even when all precautions have been taken to assure the administration of compatible blood, it must be expected that a certain number of untoward reactions will occur in both medical and surgical patients. Let us repeat what has already been said: that many reactions of minor character accompanying or following the transfusion of blood during surgical operations go unrecognized because the signs and symp-

toms engendered by the reactions have been masked by the effects of anesthesia.

When, however, an untoward reaction is manifested, it is very important to recognize it and to distinguish it from the underlying illness. During surgical operations this may be difficult, but if the physician is alert to the possibilities of such reactions they may, in most instances, be recognized. The seriousness of the situation varies according to the type of reaction which occurs. Therefore, we have felt that an attempt should be made to classify transfusion reactions so that a definite pattern of treatment for them can be set up.

At the Mayo Clinic it is the practice to divide all untoward reactions to transfusion into five categories: (1) pyrogenic, (2) allergic, (3) circulatory, (4) hemolytic and (5) a category known as "undetermined." In the last group are placed all bizarre reactions which may or may not be results of the administration of blood, but which, since blood was administered, cannot logically be omitted from possible consideration. It is possible, of course, that in maintaining such a category the transfusion of blood is sometimes wrongfully involved, but to ensure that no reaction will go unnoticed we must include those of which the cause is doubtful.

#### PYROGENIC REACTIONS

A pyrogenic reaction usually exhibits itself by a sudden chill and an increase in temperature of 1 to 4 degrees (F.); the increase in temperature appears either during or immediately after transfusion. The temperature usually will return to the level present before transfusion within four to eight hours unless something else supervenes. If this particular transfusion reaction occurs during or after an operation, the increase in temperature may be confused with the increase that ordinarily follows an operative procedure. When, however, the increase in temperature is the result of a transfusion reaction, it usually is greater than the average increase that follows the particular operation. Sometimes it may be difficult to distinguish, one from another, a very mild hemolytic reaction or a very severe chill and increase in temperature accompanying a pyrogenic reaction. The usual pyrogenic reaction does not produce free hemoglobin in the patient's serum and urine; this is one of the distinguishing differences between a hemolytic reaction and a pyrogenic reaction.

Depending on the indications for transfusion and on whether or not sufficient blood was transfused, a pyrogenic reaction usually does not interfere greatly with the desired therapeutic effect; for example, the expected increase in the quantity of hemoglobin and erythrocytes. When pyrogenic reactions are very mild, transfusion usually can be continued. When, however, they are severe, administration should be discontinued, at least temporarily.



Codeine or morphine as a sedative agent is valuable for a patient who is uncomfortable and has a chill. The external application of heat is appreciated by the patient; any further treatment is symptomatic.

#### ALLERGIC REACTIONS

An allergic reaction may occur not only in the conscious patient but also in a patient under the influence of general anesthesia. It may be very mild or extremely severe. Such reactions manifest themselves as urticaria or hives, and, if they are severe, as dyspnea, typical asthmatic rales and spasm of the smooth muscles. Still more severe reactions may resemble anaphylactic shock, which may be very quickly fatal. Fortunately, the milder forms of allergic reactions are the types most commonly seen.

Allergic reactions appear in about 1 to 3 per cent of transfusions. The exact mechanism is not known. We have observed allergic reactions in recipients of blood who never before exhibited allergic phenomena. We have also seen instances in which the same donor's blood, from the same bottle, administered to different recipients, had provoked allergic reactions in only one of the recipients, the others remaining free of any difficulty. Moreover, we have seen familial sensitivity, the recipient receiving blood from some member of his family on different occasions and becoming the victim of marked urticaria.

Occasionally, a donor has ingested a certain type of food a few hours previous to the donation of his blood. The recipient may be sensitive to that particular food and may exhibit allergic symptoms during or after transfusion.

The symptoms of an allergic reaction frequently are relieved by the subcutaneous or intravenous injection of 0.25 to 1 cc. of a 1:2,600 solution of epinephrine hydrochloride, provided that epinephrine is not contraindicated. One of the antihistaminic drugs administered to the patient during the allergic reaction is not quite so effective as it is when it is administered to the patient before transfusion was started.

If a recipient is known to be sensitive, certain precautionary measures can be taken: (1) A fasting donor can be obtained; (2) at the time of administration an adequate amount of an antihistaminic drug can be added to the bottle of donor's blood; (3) if it is deemed advisable, 0.50 to 1 cc. of a 1:2,600 solution of epinephrine hydrochloride can be added to the blood; (4) an antihistaminic drug can be administered to the patient orally or intravenously, and (5) additional treatment as found necessary can be carried out.

Occasionally, in spite of the foregoing precautions, the patient still exhibits allergic symptoms. In this event, a suspension of washed erythrocytes may be prepared. If these resuspended erythrocytes,

instead of whole citrated blood, are administered, frequently the allergic phenomena will not appear.

Despite the allergic reaction, the desired therapeutic effect usually is obtained from the transfusion.

#### CIRCULATORY REACTIONS

A circulatory reaction generally is encountered in patients suffering from some chronic cardiac disease. As a rule, the reaction is due to an overloading of the circulatory system, thus disturbing the cardiac or pulmonary mechanism. It is brought about by the administration of too great a volume of blood or the intravenous use of too large a quantity of fluids, too rapid an administration of blood or too rapid an intravenous infusion of fluids. Failure of the right side of the heart, accompanied with a decrease in blood pressure and a very rapid pulse, with sweating, pulmonary edema and cyanosis, appear. Fortunately, this complication is not seen frequently. Often when it is seen the prognosis must be guarded.

There should be no particular difficulty in making a diagnosis. Ordinarily this type of patient exhibits one of the contraindications to transfusion. If blood is to be transfused to such a patient, in spite of the contraindication, then extreme care should be exercised in administration of the blood. The first step in the treatment of circulatory reactions is prophylaxis.

When this complication does make its appearance, inhalations of oxygen under pressure are indicated. It may be necessary to withdraw from the patient an amount of blood at least equal to that administered. Spontaneous recovery may occur.

#### HEMOLYTIC REACTIONS

For more than two centuries the successful transfusion of blood has been hindered by the grave manifestations of agglutination and hemolysis, resulting from the mixing of incompatible blood. Today, hemolytic reactions still constitute one of the most serious complications with which physicians must contend.

The reaction may be the result of the administration of incompatible blood, the administration of group O blood of too high a titer to a recipient whose blood is in group AB, A or B, the administration of blood already hemolyzed or the presence of intragroup and Rh incompatibilities.

*Diagnosis.*—At times the reaction is so mild that it goes unrecognized. At other times it is severe enough to end fatally for the recipient. The clinical manifestations generally are characteristic. The reaction usually occurs early in transfusion or immediately after its

completion. The patient's first symptoms are generalized tingling, with a sense of great discomfort and anxiety; lumbar pain; a cold, clammy skin; a decrease in the blood pressure; a very thready pulse; dyspnea, and cyanosis. Air hunger may be marked. Nausea and vomiting may be prominent. If the shock accompanying the reaction is successfully treated, the next prominent symptom is jaundice.

If the reaction occurs on the operating table, with the patient under the influence of general anesthesia, it is much more difficult to recognize the untoward reaction. It has been interesting to us that on three separate occasions, and on each occasion a different surgeon operating, much the same remark has been passed: "What has happened to the patient? I can't stop the bleeding." In none of these instances did anyone know that a hemolytic reaction was occurring. This disturbance of the bleeding and clotting of the blood sometimes results from the transfusion of incompatible blood. It may be followed by the oozing of blood from the site of transfusion, from the gums or uterus or from an incision in the skin.

When this reaction occurs, a sample of blood withdrawn from the recipient early in the course of the reaction should show considerable free hemoglobin in the serum. The urine becomes dark because of the presence of free hemoglobin and a paucity of erythrocytes.

Such a reaction may be so mild that it will go unrecognized. Generally, however, this is not the case. After the initial insult, there is an interval of a few days in which the condition of the patient seems to be progressing favorably. He may eat and sleep well and be well oriented. This may be followed by a phase of restlessness and drowsiness, progressing into stupor, convulsions and coma. Renal failure and anuria are damming back the nitrogenous waste products. Generalized edema and purpura may appear. If diuresis begins, the prognosis is better, but continued anuria is disappointing.

The early chills and fever may be mistaken for a severe pyrogenic reaction. On the other hand, the uremic state may be so late in appearing that the original illness may be wrongly blamed for the condition of the patient. Occasionally, it is difficult to decide whether death is due to incompatible blood or acute cardiac failure.

**Hemoglobin in Plasma:** When a hemolytic reaction follows transfusion, a sample of the patient's blood should be withdrawn. Five cubic centimeters of blood is drawn into a tube containing 0.50 cc. of a mixture of equal parts of 6 per cent solution of ammonium oxalate and 4 per cent solution of potassium oxalate. The blood is centrifuged, and the overlying plasma is examined for free hemoglobin. This procedure must be done soon after the appearance of the symptoms, because free hemoglobin disappears very quickly from the circulation. If the sample is withdrawn too late and free hemoglobin is not found,

a false sense of security may be obtained. All free hemoglobin may have disappeared from the circulation within four to five hours. If blood that is too old or is outdated is administered, free hemoglobin may be present in the circulation for two to three hours, after which bilirubinemia occurs and fades away in twenty-four to forty-eight hours. These particular changes may exhibit no symptoms at all.

**Hemoglobin in Urine:** A sample of urine passed after the transfusion of incompatible blood is smoky red, because of the hemoglobin. Oehlecker<sup>2</sup> has stated that hemoglobinuria does not occur unless 60 to 80 cc. of blood is hemolyzed. The coincidental presence of blood in the urine (metrorrhagia, hematuria) should cause no confusion because in these conditions numerous erythrocytes will be found and anuria is not one of the complications.

**Retesting of Blood of Donor and Patient:** Retesting of the donor's and the patient's blood for grouping and Rh factor and cross matching should be done. A sample of blood from the particular bottle from which the blood was administered to the patient should be tested for the grouping and Rh factor; cross matching should be done again. The element of human error could have intervened to cause bottles or labels to become mixed, with the result that the wrong type of blood was administered to the patient.

If fresh blood cannot be obtained from the donor, it may be possible to identify a less than average level of the alpha or beta agglutinins in the recipient's serum. This low level of agglutinins may be followed in a few days by a higher than average level of alpha or beta agglutinins. In this event, it should be suspected that the patient has received some incompatible group A or B cells.

*Pathologic Considerations.*<sup>3</sup>—The exact mechanism responsible for the hemolytic reaction is not completely understood. Phagocytosis of some of the erythrocytes takes place, but most of the incompatible cells are destroyed by the specific agglutinins in the patient's serum. It is generally accepted that the renal symptoms may be caused by the deposition in the renal tubules of the hemoglobin released from the destroyed cells. When the concentration of free hemoglobin exceeds a certain level in the circulation, the free hemoglobin is passed through the kidneys. The acute damage is seen in the tubules mechanically blocked by hematuric acid crystals and casts, degeneration and destruction of the epithelial cells of the tubules and swelling and cellular infil-

2. Oehlecker, F.: Die Bluttransfusion, in Hirschfeld, H., and Hittmair, A.: *Handbuch der allgemeinen Hämatologie*, Berlin, Urban & Schwarzenberg, 1934, vol. 2, pt. 2, pp. 1513-1592.

3. Mathieson, D. R.: Personal communication to the authors. Bennett, W. A.: Personal communication to the authors.



Fig. 1.—(a) Many casts are visible in the tubules: Several are granular in nature and one is a hyaline cast; the granular casts were stained with hemoglobin pigment; the tubule epithelium is undergoing degeneration, with a small accumulation of polymorphonuclear leukocytes, but the glomerulus tufts appear normal. (b) Necrosis of the epithelium, with casts present in the tubules: A few polymorphonuclear leukocytes are also seen about the casts and in the tubules; a few of these cells are also seen in the interstitial tissues. There is edema of the interstitial tissues. Hematoxylin and eosin;  $\times 215$ .

tration of the kidney (figs. 1 and 2). Lucke<sup>4</sup> has presented a very fine explanation of this phenomenon.

The tubular obstruction in itself, however, is not adequate to produce renal insufficiency. Some other mechanism will be needed to explain the complete shutdown of renal function. Whether or not this is a vascular response to the hemoglobin by-products is open to question. This question has been thoroughly discussed by Trueta and his co-workers.<sup>5</sup>

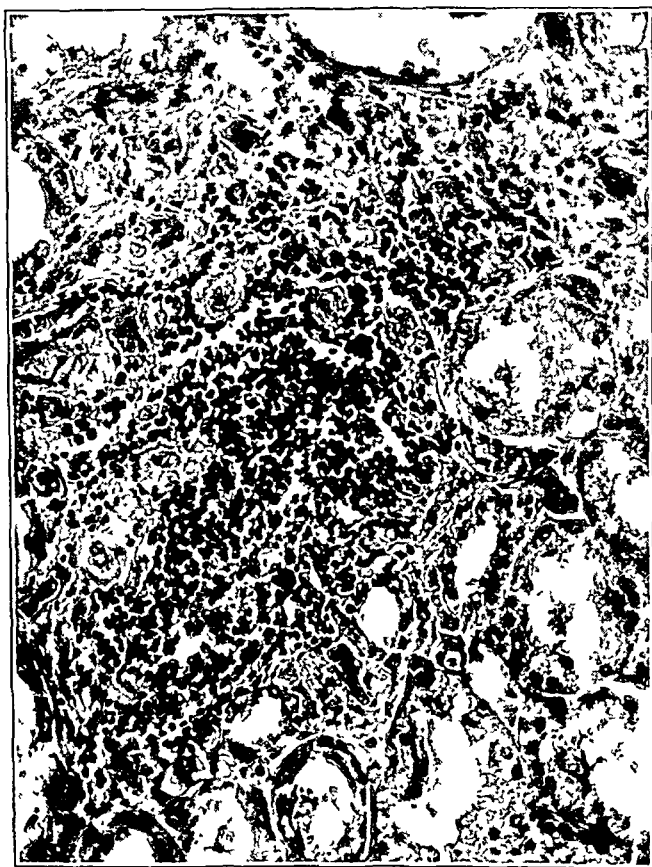


Fig. 2.—The accumulation of lymphocytes in the central area is accompanied with numerous giant cells. These giant cells contain old hemoglobin pigment. The tubules in the surrounding area are granular and swollen. This probably represents a granuloma which is in the process of picking up an old hemoglobin cast from a completely degenerated tubule. Hematoxylin and eosin:  $\times 215$ .

4. Lucke, B.: Lower Nephron Nephrosis (Renal Lesions of Crush Syndrome, of Burns, Transfusions, and Other Conditions Affecting Lower Segments of Nephrons), *Mil. Surgeon* **99**:371-396 (Nov.) 1946

5. Trueta, J.: *Studies of the Renal Circulation*, London, Oxford University Press, 1947.

Death occurring very soon after a severe transfusion reaction may reveal multiple thrombosis. When death occurs a few days later, the pathologic picture will be that already elaborated on.

*Treatment.*—In a case of suspected or proved hemolytic reaction, certain steps must be taken. In spite of the best treatment, death may follow such an untoward happening. On the other hand, the reaction may be so mild as to go unnoticed and without treatment. These steps are the following: First, if the offending blood is still running, transfusion should be stopped. Second, the patient must be supported in shock. The transfusion of known compatible blood, plasma or serum is in order. Third, the patient should be alkalinized with a 5 per cent solution of sodium bicarbonate or sixth molar sodium lactate solution. Fourth, the daily intake and output of fluids should be watched carefully. Two thousand to 3,000 cc. of fluid per twenty-four hours should be adequate. Care should be exercised that the patient does not receive too much sodium chloride. Aminophylline, human serum albumin or blood plasma may be administered to encourage diuresis. Fifth, if the patient becomes oliguric or anuric and the nitrogenous waste products are increasing, peritoneal lavage may be considered.<sup>6</sup>

#### UNDETERMINED REACTIONS

In the group of undetermined reactions, as has been said, are placed all bizarre reactions which cannot be definitely excluded as not being associated with or related to the transfusion. In such an event, the treatment must follow symptomatic lines.

#### CONCLUSIONS

The transfusion of blood is an important therapeutic method. In spite of the possibility of reactions and occasional fatalities, the proved value of the transfusion of blood far outweighs these disadvantages in most cases. Forty years ago Crile<sup>7</sup> made a very appropriate remark: "Judiciously employed, transfusion will surely prove a valuable, often life-saving resource; injudiciously used it will surely become discredited."

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6. Odel, H. M.; Ferris, D. O., and Power, M. H.: Clinical Considerations of the Problem of Extrarenal Excretion: Peritoneal Lavage, *M. Clin. North America* 32:989-1076 (July) 1948.

7. Crile, G. W.: Hemorrhage and Transfusion: An Experimental and Clinical Research, New York, D. Appleton & Company, 1909.

## DIFFERENTIAL DIAGNOSIS OF JAUNDICE IN SURGICAL PRACTICE

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IN THE past two decades, several developments have influenced our clinical thinking in regard to jaundice. Many studies of the physiology of the liver in health have been made, and laboratory methods for studying hepatic disease have been developed. The latter have tended to detract from the time-honored and thoroughly tested clinical study of the jaundiced patient. The observations on the pandemic of infectious hepatitis during World War II have emphasized the importance of the parenchymatous type of jaundice. Some sequelae of this disease, such as homologous serum jaundice—serious and often fatal—acute and sub-acute atrophy and possibly chronic atrophy or cirrhosis, remain as current problems. Radical surgical procedures have been used for the relief of obstruction due to carcinoma of the ampulla of Vater and the head of the pancreas and for the relief of portal hypertension. Recognition of pancreatitis as a more frequent and clearcut syndrome has become disseminated and incorporated with other factors in our evaluation of jaundice. The discovery and clinical use of vitamin K have added immeasurably to successful therapy of jaundice, although some factors in regard to the hemorrhagic tendency of jaundice remain unexplained.

The surgeon is interested in the patient with jaundice for several reasons. One of the most important of these is that removal of an underlying lesion may produce a cure or some palliation. He knows that such a lesion is present in many cases of jaundice. He also knows that in certain instances operation can accomplish nothing and, in fact, may be detrimental to a high degree. He thus wishes to know whether the patient with jaundice should be treated by medical or surgical means. While he is chiefly interested in therapeutics and while he usually leaves the problem of diagnosis to his medical colleague, he should be sufficiently familiar with the causes and types of jaundice and with the necessary diagnostic procedures to enable him to give an intelligent opinion when he is called in consultation. This knowledge

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From the Division of Medicine, Mayo Clinic.

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also will prevent him from knowingly or inadvertently performing an exploratory laparotomy in cases of parenchymatous jaundice and will insure that such an operation is performed in cases of obstructive jaundice.

The following statement by Moynihan has often been quoted: "No man is infallible in the diagnosis of jaundice." However, this is not a valid reason that an attempt toward infallibility should not always be made, especially since one has more tools to use in diagnosis than were available in Moynihan's day. Experience adds immeasurably to the facility with which the diagnostician arrives at his conclusions, but, no matter how great one's experience may be, medically or surgically, jaundice frequently continues to be misdiagnosed or mistreated. To lessen the number of cases in which this is true is the natural ambition of the members of the medical profession. Obviously, it is impossible to cover all details of diagnosis in this presentation; only the general principles can be outlined. Let it also be said at the outset that diagnosis should be established as early as possible in order that damage from delay in surgical treatment may be avoided and exploration of parenchymatous disease may be resisted. In the majority of instances, such diagnosis can be established reasonably, easily and early.

In approaching the problem presented by a patient with jaundice, one's orientation is influenced by certain precepts that training and experience have thoroughly ingrained in one's mental processes. Among these is a working classification of jaundice. Various classifications have been advanced, such as those of van den Bergh, McNee, Rich and Ducci. The most suitable for general clinical use would appear to be that of McNee, in which jaundice is classified as hemolytic, intrahepatic and obstructive. Although jaundice probably is never pure in type and although this classification is perhaps an oversimplification of the problem, it is a very practical one for therapeutic purposes, as it calls attention to the primary nature of the icterus.

Another precept is knowledge of the diagnostic points pertaining to the various syndromes. Hemolytic jaundice usually is readily recognized by the history, physical examination and appropriate examinations of the blood. Suffice it to say here that congenital hemolytic icterus, with its microcytic anemia, increased fragility of the erythrocytes and acholuria, is the principal example of hemolytic jaundice. It is important from the surgical standpoint because of the value of splenectomy in its management and the frequency with which gallstones are encountered in its course (60 per cent).

Intrahepatic or parenchymatous jaundice is characterized by involvement of the cells of the parenchyma and of the canaliculi. Various etiologic agents are responsible. The acute type is represented by epidemic and sporadic infectious hepatitis, homologous serum hepatitis and

toxic hepatitis, and the chronic type is represented by the various forms of cirrhosis, each with its characteristic syndrome. Pain seldom is an important feature, although at times it may be present and confusing in diagnosis. The bile ducts are patent, and rarely is there prolonged interference with the flow of bile. There usually is early and conclusive evidence of disturbance of the metabolic functions of the liver. Pruritus is not common. Intrahepatic jaundice, whether acute or chronic, is a medical problem.

Obstructive jaundice is commonly due to calculus, stricture or neoplasm and is a surgical problem. Serious disturbances of metabolic function of the liver usually are absent in the early stages. In cases in which a stone is present in the common bile duct, colic in association with the onset of jaundice is characteristic. The obstruction due to stone is seldom painless, seldom complete (perhaps in 10 per cent of cases), and the jaundice is usually mild and variable. Stone, nevertheless, may mimic any syndrome of intrahepatic or extrahepatic disease. Obstruction due to neoplasm is usually complete (90 per cent of cases), permanent and often painless. Stricture in the great majority of instances is readily recognized and follows soon after the performance of some surgical operation on the biliary tract, which is complicated by a stormy postoperative course and associated with either a deep persisting jaundice or the development of an external biliary fistula which intermittently closes and opens. Pain frequently is present, but true biliary colic is rare.

In considering the obstructive type of jaundice, the following facts should be recalled: (1) carcinoma of the gallbladder usually is associated with stones; (2) carcinoma of the head of the pancreas occasionally is associated with stones in the common bile duct or gallbladder; (3) recurrent strictures often are associated with stones above the site of obstruction, and the persisting obstruction and associated cholangitis of recurrent strictures not infrequently lead to the development of a secondary biliary cirrhosis; (4) in any case in which the obstruction persists for a month or more, secondary damage of the liver usually occurs, and (5) individual patients vary greatly in their tolerance to biliary obstruction. These facts often influence the ease or difficulty of diagnosis.

Another precept is a recognition of the relative frequency of the various types of jaundice. Published data vary considerably, depending on the type of practice they are collected from. Excluding hemolytic icterus, the majority of reports indicate that jaundice is of the intrahepatic type in from a third to a half of the cases and of the obstructive type in the remaining cases. In about half of the latter cases, the jaundice is due to benign lesions; in the remaining half, it is due to neoplasms. Obstructive lesions tend to occur in middle or later life.

and parenchymatous disease tends to occur in young persons. Gallstones are encountered more frequently in women than they are in men.

#### HISTORY AND PHYSICAL EXAMINATION

The history and the physical examination are and will remain the most important factors in the differential diagnosis of jaundice. The history is commonly developed around either the occurrence or the absence of pain. An accurate, detailed and chronologic account of the symptoms immediately or remotely preceding the onset of jaundice is most important and helpful. In cases in which the development of jaundice is associated with pain, the classic history is as follows: The patient has had chronic flatulent indigestion which has been punctuated by attacks of biliary colic which have necessitated the administration of opiates and often have been associated with chills, fever and sweats and have been followed by residual soreness and jaundice. This history is most characteristic of a stone in the common bile duct and in most instances is diagnostic. The jaundice may be mild, or even unnoticed in the early attacks. Darkening of the urine and lightening of the color of the stools may be all that the patient notices. Later, the jaundice becomes more obvious and persistent. Occasionally, it becomes deep and persistent owing to complete obstruction from impaction of the stone. While this classic history is the usual one in cases of stone in the common bile duct, the jaundice may begin painlessly (5 per cent of cases); colic may have occurred weeks or months prior to the onset of jaundice, and colic may be atypical in site and character (15 to 20 per cent of cases) or may develop after the onset of jaundice. While the colic is characteristic of a stone in the common bile duct it may occur in other conditions but is then more likely to be atypical in nature. These other conditions include carcinoma of the head of the pancreas, pancreatitis, cirrhosis and even the different types of hepatitis. At the onset of jaundice due to a malignant lesion, pain usually is absent in 40 per cent, mild in 35 per cent and severe or colicky in 25 per cent of the cases respectively. The severity of pain may be difficult to interpret. Some patients have a tendency to exaggerate; others have a tendency to minimize the severity of the pain. The latter is particularly true of the aged persons who have previously enjoyed good health and who may describe the pain of biliary colic as an attack of indigestion consisting of bloating and vomiting.

In cases in which an operation has been performed previously, it is important to inquire about the preoperative course of the illness, the surgical findings, the type of operation and the postoperative course. If a cholecystostomy only has been performed, usually for empyema of the gallbladder, persistence of jaundice obviously indicates an incomplete operation. If a cholecystectomy has been performed, persistence

of jaundice, the development or persistence of an external biliary fistula or the occurrence of colic, chills, fever and sweats and an increase in the jaundice usually mean an overlooked stone in the common bile duct, although these symptoms occasionally are due to an overlooked carcinoma of the head of the pancreas or of the ampulla of Vater or to pancreatitis. However, if jaundice had been absent before cholecystectomy was performed but develops during a stormy postoperative course and becomes deep and persistent or if the operation is followed by an external biliary fistula that closes intermittently in association with pain, fever and deepening of the jaundice, it usually may be assumed that the common bile duct has been injured.

In taking a history in a case in which jaundice has begun without abdominal pain, one should attempt to determine (1) whether or not the patient recently has been exposed to an epidemic of infectious hepatitis; (2) whether or not he recently has received any parenteral therapy, such as transfusion of whole blood or pooled plasma; (3) whether or not he recently has had an infection of the respiratory or gastrointestinal tract; (4) whether or not he recently has ingested any medicinal substance or has been exposed to any other toxic substance which might have caused injury of the liver, and (5) whether or not he recently has had a malignant tumor removed or has had any general symptoms which might indicate the development of an unsuspected malignant tumor.

In acute hepatitis, slight fever, malaise, anorexia, nausea and even vomiting may precede the onset of jaundice. In cirrhosis, the first symptom may be sudden hematemesis or the onset of ascites. In many cases of painless jaundice, there are no significant preceding symptoms. A history of premonitory or accompanying symptoms may not necessarily be diagnostic of the type of jaundice, but it may furnish circumstantial evidence or may even be misleading. For example, malignant disease may cause jaundice in the midst of an epidemic of hepatitis. Absence of historical data leaves the situation indeterminate, and the diagnosis will have to depend on physical data and laboratory procedures, with or without a period of observation.

The presence or absence of pruritus is not diagnostic. However, pruritus has a definite tendency to occur in cases of obstructive jaundice, especially if the biliary obstruction is high grade. It is often absent in the mild jaundice associated with a stone in the common bile duct, and it is occasionally absent in cases of complete biliary obstruction. In intrahepatic disease, it does not occur frequently, even if the disease is severe, and when it is present it is not often severe. It is often severe in cases of cirrhosis, especially primary biliary cirrhosis.

Physical examination may permit a definite diagnosis to be made, or it may be of little value in the diagnosis of jaundice. Special atten-

tion should be given to the size and consistency of the liver and spleen, to the presence of a palpable gallbladder, to evidence of carcinoma elsewhere and to the presence of vascular spiders. Hepatomegaly is not often diagnostic; however, marked enlargement of the liver is most suggestive of carcinoma. If the surface of the liver presents definite hard nodules, a malignant lesion almost certainly is present. A palpable distended gallbladder in the absence of inflammation nearly always means neoplastic obstruction of the common bile duct below the junction of the cystic duct and can be demonstrated clinically in 60 per cent of cases in which there is such an obstruction. When demonstrable, it is one of the most diagnostic of all physical findings. Chronic inflammatory disease of the gallbladder or previous cholecystectomy or obstruction above the junction of the cystic duct and common bile duct obviously prevents this finding. The gallbladder may be distended but not palpable if the abdominal wall is obese, muscular or unrelaxed or if an overhanging edge of the liver interferes with adequate examination. An enlarged, hard, nodular gallbladder suggests a malignant lesion of this organ.

Other physical findings worthy of note are (1) tumors elsewhere in the body, particularly in the region of the pancreas, supraclavicular lymph nodes and rectal shelf; (2) spider angiomas, which have been said to be the trademark of cirrhosis; (3) collateral venous circulation in the abdominal wall and esophagus; (4) abdominal scars and fistulas; (5) factitial dermatitis; (6) melanosis of the skin; (7) xanthomas; (8) edema; (9) ascites; (10) pallor, and (11) ecchymosis or other evidence of bleeding. Mention also should be made of the tint of the jaundice. The golden yellow or orange color of the skin most frequently seen in hepatocellular disease is often in marked contrast to the green hue of obstructive jaundice. This difference in color is not invariable and is not accepted as diagnostic in all quarters, but when present it furnishes a clue to the pathologic condition that is present.

#### PATENCY OF THE BILE DUCTS

After the history and physical examination, establishment of patency or occlusion of the bile ducts is the next important step in the diagnosis of jaundice. In some cases, this may already be evident, and no further diagnostic procedure may be indicated. However, in cases of deep painless jaundice, further investigation is necessary. Visual examination of the stools is of little aid if the jaundice is deep. The stools may appear acholic whether or not the jaundice is due to obstruction or intrahepatic disease. Chemical examination of the feces for urobilin is equally unreliable. There are, however, two fairly satisfactory procedures which are useful in establishing patency or obstruction of the bile ducts. These are duodenal intubation and quantitative determina-

tion of the urobilinogen in the feces. When duodenal intubation is performed, the position of the tube should be checked by roentgenologic examination if no bile is obtained. Recovery of bile means that the liver is secreting bile and that the bile ducts are at least partially patent. Failure to obtain bile indicates either complete obstruction of the bile ducts or complete suppression of the secretion of bile at the time of intubation. The latter rarely persists long, if it actually occurs, and bile is usually obtained if the intubation is repeated a few times. If bile is persistently absent, complete and permanent obstruction is usually present. Duodenal intubation may serve a further useful purpose. The recovery of gross blood is suggestive of an ampullary lesion or of a carcinoma of the pancreas which is ulcerating into the duodenum.

Determination of the urobilinogen content of the feces should be carried out with great care. Collection of the feces for at least seventy-two hours is necessary. The determination should be repeated from time to time during the period of observation to determine whether permanent obstruction of a bile duct or temporary suppression of bile is present.

In cases in which jaundice is caused by a malignant lesion of the extrahepatic biliary tract, the bile ducts usually are completely and permanently occluded, whereas in cases of parenchymatous jaundice they are patent. Duodenal intubation and quantitative determination of the urobilinogen in the feces are used to determine this obvious and fundamental difference between the two types of jaundice. Exceptions to these findings occur under the following conditions: 1. In an occasional case of malignant disease, the obstruction may be incomplete and suggest the presence of parenchymatous jaundice. 2. In an occasional case of malignant disease, complete obstruction may become incomplete and the jaundice may tend to disappear; as a result, the presence of parenchymatous jaundice may be suspected. 3. In an occasional case of severe parenchymatous jaundice, especially in the first ten to fifteen days, there may be nearly complete suppression of the secretion of bile and the presence of complete obstruction may be suspected.

#### ROENTGENOLOGIC EXAMINATION

Roentgenologic examination seldom furnishes conclusive diagnostic data in cases of jaundice. Cholecystography has little to offer in cases of jaundice, and the results of this procedure may be misleading. Occasionally, it reveals a primary shadow of the gallbladder, which indicates disease of this organ. In some instances, roentgenograms of the upper part of the abdomen may demonstrate biliary or pancreatic calculi. However, in the presence of deep, painless jaundice, the demonstration of a stone or stones in the gallbladder should not be interpreted as

necessarily indicating the presence of a stone in the common bile duct. The possibility that the jaundice may be due to a malignant lesion or to primary parenchymatous disease of the liver should not be ignored. Indeed, either of these is more likely than a stone in the common bile duct. Roentgenologic examination of the esophagus, stomach and intestine is valuable in demonstrating the presence or absence of esophageal varices and intrinsic malignant lesions. Occasionally, widening of the duodenal loop may indicate enlargement of the head of the pancreas. Cholelithograms are useful in studying biliary fistulas or patency of the bile ducts if a drainage tube is situated therein.

#### CHEMICAL EXAMINATION AND TESTS FOR HEPATIC FUNCTION

The first, and probably the most important, chemical examination which should be performed in any case of jaundice is the measurement of the amount of bilirubin in the serum. This is done best by use of the van den Bergh reagent, although the determination of the icterus index may be utilized. Several satisfactory procedures for the former are available. The presence of direct-reacting bilirubin in the serum does not differentiate hepatogenous from obstructive jaundice. Furthermore, the amount of direct-reacting bilirubin cannot be commonly used for this purpose, because it is increased in both intrahepatic and obstructive jaundice. The quantitative determination of serum bilirubin, however, furnishes some information that is of definite value in determining (1) the degree of icterus; (2) the course of the jaundice, if repeated determinations are carried out, and (3) the cause of the icterus. If the concentration of serum bilirubin is 12 to 20 mg. per hundred cubic centimeters, it indicates either complete obstruction or severe hepatogenous icterus; if it is higher than 25 mg. per hundred cubic centimeters, it indicates severe parenchymatous disease, which is usually primary but may be secondary to obstruction. Concentrations which are less than 10 mg. per hundred cubic centimeters usually mean that any obstruction present is not complete.

The remaining chemical tests are usually described as liver function tests. They have been developed partly to aid in distinguishing obstructive jaundice from parenchymatous jaundice but chiefly for studying disturbances of the metabolic functions of the liver. Their multiplicity and the constant addition of new tests indicate that no single test or combination of tests is entirely satisfactory. Some of these tests have been utilized by Watson as part of his "profile" study of jaundice. The table shows the results of some of these tests in cases of obstructive jaundice and in cases of parenchymatous jaundice. Their use is based on the fact that in cases of obstructive jaundice a disturbance of metabolic function seldom occurs unless the jaundice has been present

for a long time or is complicated by infection, whereas in cases of parenchymatous jaundice a definite disturbance of metabolic function usually becomes evident early in the course of the disease. They are not intended as a substitute for clinical study and judgment, but they may extend the range of accuracy of diagnosis. Some of them are generally accepted as a necessary and important part of the study of cases of jaundice.

The value for plasma cholesterol is increased in about 80 per cent of cases of obstructive jaundice, while it is normal or decreased in about 90 per cent of cases of primary parenchymatous jaundice. However, major exceptions may be encountered, such as an increased value in cases of parenchymatous jaundice and a normal or low value in cases of obstructive jaundice. Normally, more than 50 per cent of the plasma cholesterol is combined with fatty acids. Low values for cholesterol esters are most frequently obtained in cases of primary disease of the

*Results of Tests of Hepatic Function in Cases of Obstructive Jaundice and Parenchymatous Jaundice*

Test	Results	
	In Obstructive Jaundice	In Parenchymatous Jaundice
Concentration of plasma cholesterol.....	Increased	Normal or decreased
Concentration of serum alkaline phosphatase.....	Increased	Normal
Cephalin-cholesterol flocculation .....	Negative	Positive
Thymol turbidity .....	Negative	Positive
Effect of vitamin K on prothrombin time.....	Prompt	Delayed or absent

liver, the degree of lowering being roughly indicative of the degree of parenchymatous damage.

Earlier investigators of the value of serum alkaline phosphatase claimed that values above 10 units (Bodansky) strongly supported the presence of an obstructive type of jaundice and values below 10 units indicated the presence of a hepatogenous type of jaundice. Later investigators became skeptical of the diagnostic value of the concentration of the serum alkaline phosphatase because of the many exceptions. Nevertheless, alterations in the value for the serum alkaline phosphatase, taken in connection with other findings, may be of considerable help in differential diagnosis.

The cephalin-cholesterol flocculation test of Hanger and the thymol turbidity test of Maclagen are dependent on alterations in the serum proteins and lipids. Definitely positive reactions in the presence of deep jaundice usually mean active destruction of the hepatic parenchyma. Because of this, positive results with these tests usually are obtained early in acute and subacute hepatitis and late in obstructive jaundice. However, exceptions occur; negative results, for some



unknown reason, are at times obtained in parenchymatous disease and positive results may be encountered in obstructive jaundice. The results must be correlated with other data. Nevertheless, in cases of deep jaundice, when operation is being considered, a positive thymol turbidity test should not be ignored. It should necessitate a careful review of all other data.

The prothrombin time should be determined in every case of jaundice and in every case of disease of the liver. If it is increased, a prompt return to normal on administration of vitamin K is indicative of obstructive jaundice, whereas its failure to return to normal or a slow return to normal indicates failure of utilization of vitamin K, which is the result of serious hepatic injury.

In general, the pattern revealed by these tests in cases of obstructive jaundice is characterized by an increase in the concentration of both plasma cholesterol and serum alkaline phosphatase, a negative cephalin-cholesterol flocculation reaction, a negative thymol turbidity reaction and a prompt response of the hypoprothrombinemia to vitamin K. In cases of parenchymatous jaundice, the pattern is characterized by a decrease in the concentration of both cholesterol and cholesterol esters in the plasma, a concentration of serum alkaline phosphatase of less than 10 units (Bodansky), a positive cephalin-cholesterol flocculation reaction and a positive thymol turbidity reaction. The response of hypoprothrombinemia to the administration of vitamin K usually is delayed, although it may be absent or occasionally prompt. In cases of chronic disease of the liver, the concentration of serum albumin is decreased and that of the serum globulin is increased. In an appreciable percentage, perhaps 20 per cent, of cases of parenchymatous disease of the liver, the results of these tests are normal or resemble those obtained in cases of obstructive jaundice. This has been explained on the basis that the hepatic lesion involves the cholangioles rather than the polygonal cells. On the other hand, in some cases of obstructive jaundice the results of these tests resemble those usually obtained in cases of parenchymatous jaundice. In such cases, the obstruction usually has been present for a long time or a parenchymal change has occurred as a result of the obstruction.

#### COMMENT

A careful study of the clinical history, the physical findings and the results of tests for patency of the bile ducts and for hepatic function will result in a positive diagnosis in 80 to 90 per cent of cases of jaundice. In the remaining small percentage of cases, there may be reasonable doubt in regard to diagnosis. The history may be confusing, the physical findings meager and laboratory data equivocal. In the individual case, theory and the clinical and laboratory findings may

not coincide. Evidence may be conflicting. The most troublesome cases are those in which the onset of jaundice is painless. In such cases, parenchymatous jaundice may be confused with malignant obstruction, especially if the obstruction is incomplete. Some physicians would consider all such cases of painless jaundice as cases of parenchymatous disease until proved otherwise, particularly in view of the recent pandemic of infectious hepatitis. In the majority of cases of parenchymatous jaundice, the icterus will disappear in two to eight weeks. In cases of obstruction, the jaundice will persist.

In cases of parenchymatous jaundice, exploratory laparotomy may lead to serious results. On the other hand all are aware of the occasional case of painless jaundice in which relief is obtained by the removal of gallstones which have been silent and overlooked. In such cases, however, no harm will result from keeping the patients under careful observation for a reasonable time, at least until it is determined that acute or subacute hepatitis is not the basic disorder. Few surgeons have not had the experience of inadvertently performing a laparotomy in a case in which medical treatment was indicated, and few internists cannot count among their cases some in which the patients have been denied a curative operation. Such errors are usually due to a hurriedly taken or incomplete history, to overlooking something on physical examination, to inadequate laboratory investigation, to misinterpretation of data or to insufficient observation. It may be necessary to check and recheck the history, never forgetting that useful information may be obtained from the family or the family physician. A repeated physical examination may reveal some new findings that may clinch the diagnosis. Judicious repetition of some laboratory tests from time to time may be illuminating. One always should keep in mind the relationship of the time factor in cases in which some of the tests for hepatic function subsequently furnish useful information. Experience assists clinical judgment and may permit some short cuts in diagnosis, but, in general, it is not wise to pursue these too far. It is like the master of a ship directing his vessel without carefully charting his course and observing all possible bearings.

In conclusion, it is desirable to state some of the surgical indications and contraindications in conditions associated with jaundice. The former include (1) a reliable history of gallstones or colic or both; (2) proved intermittent biliary obstruction, usually due to a stone in the common bile duct but occasionally due to stricture or to both stricture and a stone and indicated by fluctuating jaundice, colic, fever and chills; (3) proved complete and permanent biliary obstruction, usually indicative of a malignant lesion; (4) an external biliary fistula, either intermittent or persistent, usually indicating a stone in, or a stricture of,

the common bile duct or both a stone and a stricture, and (5) painless jaundice appearing within six months after cholecystectomy and usually due to traumatic stricture, provided serum hepatitis is not present.

These indications may be considered conservative, and the surgeon may properly decide to proceed with operative intervention on much less definite ground. Whether the indications are clear or not, the following relative contraindications should always be given consideration in making the decision. These are directed at the avoidance of surgical procedures in cases in which jaundice is caused by injury to the parenchyma of the liver alone and include (1) recent exposure to hepatotoxic agents and infectious hepatitis and transfusion of plasma or whole blood within two to four months; (2) signs of serious hepatic disease, such as vascular spiders, visible collateral circulation, edema and pronounced hypoproteinemia; (3) intense jaundice (serum bilirubin in excess of 25 mg. per hundred cubic centimeters with patent biliary passages; (4) decidedly chronic jaundice with splenomegaly, a condition formerly described as primary biliary cirrhosis and more recently as cholangiolitic cirrhosis; (5) hypoprothrombinemia that is refractory to vitamin K, and (6) a positive result of a thymol turbidity test.

#### SUMMARY

When a detailed chronologic history has been taken, a careful physical examination made and patency or occlusion of the external biliary tract established in a case of jaundice, it is possible in the majority of instances to classify with considerable confidence the jaundice into one of the three fundamental groups: hemolytic, intrahepatic and obstructive. It also is possible to clarify the surgical indications or contraindications and to determine whether the jaundice due to obstruction is the result of a stone, a stricture or a malignant lesion. Laboratory investigation may lend material assistance in confirming the clinical diagnosis, may be actually diagnostic or may warn of danger in performance of an exploratory operation and indicate a delay. In a small group of cases, the diagnosis may remain uncertain and a period of further observation with a careful review of all data and judicious repetition of some of the laboratory procedures may be in order. Even then in a few instances an exploratory laparotomy may be necessary before the diagnosis can be established with certainty. Mistakes of both commission and omission are usually the result of failure to secure all obtainable data, of attempted short cuts and of misinterpretation of data. If strict adherence to established tenets and procedures is maintained, the differential diagnosis of jaundice can be approached with confidence and success and the surgical indications can be thoroughly clarified.

## DISCUSSION OF PRECEDING PAPERS

DR. FORRESTER RAINE, Milwaukee: In reference to Dr. Seldon's discussion of hemolytic reactions, I think one might consider an additional form of treatment that he did not mention. I had occasion recently to be interested in a patient who received 500 cc. of incompatible blood, when my associate who is in charge of the transfusion service was called in to take care of her. She did not get a very violent clinical reaction, but in twelve hours it was noted that her urine was absolutely black and her blood at this time was black also. She had had an output of only 200 cc. of urine at the end of twelve or fourteen hours after her operation.

An exsanguination transfusion was done, removing and giving her 12 pints (5.7 liters) of blood. At the close of that time her blood, which had been black at the start, was of a rather good red color and her urine began to increase in amount almost at once and was pretty clear immediately afterward; by the next day it was entirely normal. The patient made an uneventful convalescence.

It seems to me that one can assume that renal damage does not necessarily occur all at once in these instances but is progressive, and possibly, if enough of this agglutinated hemolyzed blood can be removed, we may prevent sufficient damage to the kidney to produce anuria, which did not develop in this patient.

DR. WALTER G. MADDOCK, Chicago: I should like to ask Dr. Ravdin to say a few words on his experience with the intravenous use of hydrolysate solutions and their possible benefit in relation to this work on hepatic damage.

DR. I. S. RAVDIN, Philadelphia: The question of the nutritional state of the patient is one that we have been interested in for some time, and we have belatedly come to the conclusion that the best way to feed a patient is by mouth. There is no known method now of intravenous therapy which will satisfy all the nutritional requirements of the patient over a period of time. One can, if the oral method is not available, save the patient considerably by intravenous therapy, but there is no indication that would permit one to draw any conclusion other than that such therapy is extravagant and wasteful when the oral method is available. Nitrogen balance studies mean little unless one knows that the nitrogen has been used in the protein pool of the body. For instance, one can give gelatin intravenously and produce a positive nitrogen balance, but one well knows that large amounts of the gelatin are stored in the body as gelatin and naturally therefore the patient may actually be in negative nitrogen balance. The same is true of the use of human serum albumin which is not readily used in the protein pool of the body. The evidence which Dr. Liegel and her group in our laboratories obtained is exactly similar to the evidence reported by Dr. Madden, that one can obtain positive nitrogen balance with a smaller amount of nitrogen by mouth and with somewhat less calories than one can if one attempts to produce a similar circumstance by intravenous feeding in man. There can be no doubt but that when one is attempting to produce regeneration of the liver in man, one must take into account not only the composition of the diet but also the fact that over a period of days in the preoperative period the patient must ingest a large number of calories—3,500 to 5,000 calories a day. This cannot be obtained by any other means than providing the patient with the dietary which the patient will eat. We are convinced that if such a dietary is provided by mouth—and usually patients will eat it—it had best be a complete dietary of whole components of foodstuffs, rather than predigested protein.

There is some reason to believe that if the liver on the verge of incompetency has thrown into it large amounts of predigested components that liver may be thrown into incompetency. We are not entirely sure of the latter fact, but the

problem of distention and its effect on the liver was found during experiments designed to test that very problem.

DR. J. DEWEY BISGARD, Omaha: What if one had to depend on another route—if the oral route was not available or usable? What would be your routine in maintaining nutrition?

DR. I. S. RAVDIN, Philadelphia: We would use just exactly what every one of you uses then, the substances that are available, the protein hydrolysates and glucose. We have from time to time used various fat preparations that have been prepared for us. We have not as yet had a satisfactory stable preparation for the injection of fat by the intravenous route, but we should increase our total caloric intake if we had such a preparation readily available by the utilization of fat, and in these circumstances, if one introduces a sufficient amount of split protein which contains a sufficient amount of thiamine—and especially choline—one would not expect the amount of lipid in the liver to increase.

DR. T. H. SELDON, Rochester, Minn.: I was interested in the remarks of Dr. Raine. In the Institute of Experimental Medicine, Mayo Foundation, a Fellow is working on a project whereby it is hoped to be able to transfer the blood of 1 animal to a second animal by a continuous pump system. The second animal, it is hoped, will be able adequately to look after the needs of renal excretion for both animals. To date this work has not been completed. From a clinical point of view we have thought of the possibility of doing exsanguination transfusions on patients. I am interested to know that this has been carried out successfully in practice.

## RETROGRADE SPREAD OF CARCINOMA IN THE RECTUM AND RECTOSIGMOID

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SINCE knowledge concerning the frequency, extent and nature of retrograde spread<sup>1</sup> of carcinoma in the rectosigmoid and rectum is still incomplete, many surgeons are uncertain of the surgical procedures offering the most promise to the patient. However, those surgeons who are most radical in their practice point to a lesser number of recurrences in patients so treated when compared to those who have been less radically treated. The question therefore arises of whether increased incidence of recurrence in the less radically treated patients may not be due to preoperative retrograde spread from the portion of the bowel removed to the portion left behind.

Attempts to answer this question appeared in the literature of 1913 and 1914.<sup>2</sup> It was shown that in approximately 20 specimens retrograde spread occurred from 1 to 2 cm. below the lesion. However, the method of study was inadequate since examination was limited to a strip of bowel 1 cm. wide and 20 cm. long cut into approximately twenty 1 cm. blocks, from each of which one section had been cut for microscopic examination.

During the next twenty-five years investigators<sup>3</sup> dissected lymph nodes below the primary lesion and sectioned them serially. Of 607 specimens thus examined retrograde spread was observed in 45. Five of these 45 showed tumor from 2 to 7 cm. below the lesion. The

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From St. Vincent's Hospital.

1. We are using the term "retrograde spread" in the sense of the tumor spreading from the primary lesion down in the direction of the anal canal within the wall of the bowel or into immediately adjacent lymph nodes.

2. Cole, P. P.: *Brit. M. J.* **1**:431-433, 1913. Monsarrat, K. W., and Williams, I. J.: *Brit. J. Surg.* **1**:173-182, 1913. Cheatle, G. L.: *Brit. M. J.* **1**:303, 1914.

3. Collier, F. A.; Kay, E. B., and MacIntyre, R. S.: *Surgery* **8**:294-311, 1940. Dixon, C. F.: *Am. J. Surg.* **46**:12-17, 1945. Gilchrist, R. K., and David, V. C.: *Ann. Surg.* **108**:621-642, 1938. Glover, R. P., and Waugh, J. M.: *Surg., Gynec. & Obst.* **82**:434-448, 1946. *ibid.* **82**:438, 1946. Grinnell, R. S.: *Ann. Surg.* **116**:200-216, 1942.

Case No.	1153	S-650	A-2545	S-2131	S-2125	S-1836	S-1999	S-1830	S-1753
Duration clinically, months.....	3	5	?	4	12	4	3	4	3
Site of main lesion.....	Anterior right lateral wall	Posterior wall	Anterior wall	Anterior lateral wall	Anterior wall	Left anterior wall	Posterior wall	Posterior wall, sacrum	Posterior wall
Distance above anal ring, cm.....	8.5	2	20	11	7.6	11	10.5	6	7
Size .....	2 x 1 cm.	5 x 4.2 cm.	6 x 2.6 cm.	5.4 x 4 cm.	6 x 6 cm.	4 x 4 cm.	4.2 x 4.8 cm.	6 cm. long	4 x 6 cm.
Distance short of complete element, cm.	4	1.6	1.8	1.4	1.8	1.2	0.8	2 x 2 cm.	4.4
Microscopic appearance.....	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma with mucoid degeneration	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
Group .....	C	C	C	C	B	C	C	C	C
Multiple lesions.....	0	0	Benign papilloma	0	Duke C tumor,* 5.2 cm. downward	0	0	0	0
Downward extension.....	Direct extension,* 3 cm.; node, 7 cm.	0	4.5 cm.*	0	0	0	0	Direct extension,* 6 cm.	0
Peritoneal invasion.....	0	0	Present	0	0	0	0	0	0
Levator ani.....	0	0	0	0	0	0	0	Present	0
Paraortic node.....	0	0	0	0	0	0	0	0	0
Liver .....	One small nodule seen	0	0	0	0	0	0	0	0
Lungs .....	0	0	0	0	0	0	0	0	0
Number of sections.....	200	40	200	200	170	520	170	40	220

\* See figures 1, 2, 3 and 4.

inadequacy of this second method is obvious, since there was no thorough examination of the wall of the bowel itself. We therefore attempted to secure a more complete examination by using a serial section method which embraced the entire circumference of the wall of the bowel. It is the result of this study which we wish to present.

In the accompanying table the essential clinical and pathologic data are condensed.

Nine specimens were studied. Eight were obtained at operation and 1 at autopsy. These were photographed, measured and then drawn to scale. After fixation in 4 per cent formaldehyde the whole bowel was sectioned transversely from the lower margin of the tumor to the upper level of the anal ring, in approximately 0.5 cm. blocks. A single microscopic section, made from the proximal surface of each block, served to screen the various levels for tumor. Specimen 1836, the first to be studied in this series, was cut 5 microns in thickness at 100 micron intervals. All subsequent specimens were cut at 250 micron intervals unless screening exhibited involvement, in which instances sections were cut at 100 micron intervals. One thousand, eight hundred slides were thus prepared.

#### RESULT OF STUDY

All tumors were ulcerated, cylindric cell adenocarcinomas. One showed colloid degeneration. Eight were classified as Duke C tumors, and one as a Duke B tumor (see table).

In 5 specimens there was no retrograde spread. One specimen showed retrograde extension for 6.4 cm. below the main lesion (case 3). Another specimen was seen to have a second tumor of microscopic size 6 cm. below the main lesion. In 2 others there was extensive retrograde involvement of lymph channels and lymph nodes for significant distances below the primary lesion.

CASE 1 (no. 1153).—A man aged 63 had symptoms for three months. A tumor was found 8.5 cm. above the anal ring, encircling all but 4 cm. of the total circumference. It was adenocarcinoma, Duke C. Serial section revealed narrow columns of tumor extending below the main tumor for 3.4 cm. within the submucosa and muscularis. This downward extension was not grossly detectable, the mucosa covering it being intact. In addition to this, numerous lymph channels of the submucosa, muscularis and serosa, distended with tumor, were found as low as 7 cm. from the inferior margin of the primary lesion (fig. 1).

CASE 2 (no. 2545).—The patient was a man aged 76. The duration of his disease was unknown. A carcinoma which involved all but 1.8 cm. of the circumference was found 20 cm. above the anal ring. Microscopic examination proved it to be a cylindric cell adenocarcinoma with colloid degeneration. Study of the serial sections revealed many tumor nodules of microscopic size in the adventitia, scattered downward for a distance of 4.2 cm. below the inferior





Fig. 1 (case 1).—Lymph channels lying within the intermuscular connective tissue are filled with tumor. (Level is 5 cm. below the inferior border of the main lesion )



Fig. 2 (case 2) —Lymph channels in the serosa are distended with malignant cells. These were found as low as 42 cm below the inferior margin of the main lesion

margin of the primary lesion (fig. 2). There were in addition many tumor-distended lymph channels in the submucosa, muscularis and adventitia.

CASE 3 (no. 1830).—The patient was a man aged 76. The tumor occupied the entire circumference of the wall of the bowel in the rectum 6 cm. above the



Fig. 3 (case 3).—Tumor infiltration in the submucosa extending down for a distance of 4.1 cm.

anal ring. It was an adenocarcinoma, Duke C. Study of the serial sections revealed a 2 cm. wide direct extension downward from the inferior margin of

the main lesion for a distance of 4.1 cm. The area of extension lay entirely within the submucosa and muscularis (fig. 3). Lymph nodes and lymph channels subjacent to this narrow zone of extension were involved by tumor. Many hyperplastic lymph nodes were noted below the main tumor. Below the main tumor and lateral to the retrograde extension many hyperplastic lymph nodes were noted, but none was involved by metastasis.

CASE 4 (no. 2128).—The patient was a woman aged 60. The rectal tumor was found on the anterior wall 7.6 cm. above the anal ring and fell 1.8 cm. short



Fig. 4 (case 4).—Lymph channel in the tunica propria filled with carcinoma. Lymph channels such as these were found between the two tumors. None was found below the small tumor.

of completely encircling the wall of the bowel. Microscopically it proved to be adenocarcinoma, Duke B. On study of serial sections, a small tumor 3 by 2 mm. was found in the mucosa 5.2 cm. below the large primary tumor. It was an adenocarcinoma. Many lymph channels in all layers of the wall of the bowel between the large and the small tumor were filled with tumor cells (fig. 4). Serial section below the second microscopic tumor failed to show retrograde spread.

## COMMENT

Although the total number of cases in the present study is small, it nevertheless shows that in cases of moderately advanced carcinoma of the rectum retrograde spread is common. Demonstration of this fact, however, proved laborious since serial section was necessary. It is not our purpose to establish case 4 as an example of multiple primary carcinoma of the rectum. Of greater significance is the fact of its presence. It would be of interest to know how often this circumstance might be found if a large series of specimens were studied by our method.

An attempt to correlate duration of symptoms with presence or absence of retrograde spread would be interesting, but the small number of our cases would make conclusions precarious. Suffice it to say that in 1 instance of retrograde spread symptoms were present for three months and in another case for twelve months.

Since we were primarily interested in spread downward we did not section the bowel above the site of the tumor as carefully as we did that below the tumor; hence we are not in a position to state categorically that retrograde spread was or was not related to complete block of lymph channels in the forward position.

We feel that our findings support the surgeons who use radical procedures. Though our conclusion is based on a relatively small number of cases, it is nevertheless worthy of consideration because of the complete and laborious examination of the material.

## EARLY AND DELAYED CLINICAL EFFECTS OF VAGOTOMY FOR PEPTIC ULCER

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**B**ETWEEN Nov. 1, 1946 and Nov. 1, 1947, vagus resection for treatment of peptic ulcer, as recently advocated by Dragstedt,<sup>1</sup> was performed in 42 cases at the Veterans Administration General Hospital at Los Angeles (Sawtelle), Calif. All patients were operated on by surgeons of the joint graduate teaching service of the University of Southern California, College of Medical Evangelists, and the University of California at Los Angeles medical schools. The patients, all men, varied in age from 20 to 68 years, the average age being 47½ years. One or more of the classic indications for surgical intervention in treatment of peptic ulcer were present in all cases, namely, (1) chronicity with poor response to, or inability to carry out, an adequate medical regimen, (2) hemorrhage and (3) obstruction. The duration of symptoms varied from four months to twenty years, the average being 11.2 years. Recurrent or intractable pain was a prominent feature in the majority of these cases. Hemorrhage, as determined by a history of hematemesis or melena, was present in 16 cases, together with other symptoms, but did not in itself constitute an indication for vagus resection in this series. Obstruction, as determined by retention of barium after six hours during roentgenologic study, was present in 8 cases. Twenty-four patients had undergone previous operation for treatment of peptic ulcer. These

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1. (a) Dragstedt, L. R., and Owens, F. M.: Supradiaphragmatic Section of Vagus Nerves in Treatment of Duodenal Ulcer, *Proc. Soc. Exper. Biol. & Med.* **53**:152-154, 1943. (b) Dragstedt, L. R., and Schafer, P. W.: Removal of the Vagus Innervation of the Stomach in Gastroduodenal Ulcer, *Surgery* **17**:742-749, 1945. (c) Dragstedt, L. R.: Vagotomy for Gastroduodenal Ulcer, *Ann. Surg.* **122**:973-989, 1945.

included 15 patients with perforation treated by simple closure, 7 who had undergone previous gastroenterostomy and 3 who had been subjected to previous partial gastrectomy. Four patients had undergone multiple previous operative procedures; perforation had occurred twice in 2, and 2 others had been subjected to repair of perforation followed at a later date by gastroenterostomy.

In this series, transthoracic vagus resection was done in 9 cases, abdominal vagotomy without any complementary procedure in 13 cases, vagotomy plus gastroenterostomy in 14 cases and vagotomy plus subtotal gastric resection in 6 cases. There was no apparent indication for the particular type of approach or procedure with the exception that complementary gastroenterostomy or gastrectomy was performed in each of the 8 patients who showed preoperative evidence of pyloric obstruction. Table 1 summarizes the data on all vagus resections done at this institution from Nov. 1, 1946 to Nov. 1, 1947.

TABLE 1.—*Data on Resection of Vagus Nerve Done from Nov. 1, 1946, to Nov. 1, 1947*

Type of Operation	Number of Cases	Duodenal Ulcer	Gastric Ulcer	Gastro-jejunal Ulcer
(1) Vagus resection only				
(a) Transthoracic.....	9	5	0	4
(b) Abdominal.....	13	6	1	6
Total.....	22	11	1	10
(2) Vagus resection plus gastroenterostomy....	14	14	0	0
(3) Vagus resection plus partial gastrectomy...	6	6	0	0
Total number of cases.....	42	31	1	10

#### EARLY POSTOPERATIVE STUDIES

The early postoperative course of these patients was followed prior to their discharge from the hospital with regard to subjective relief of symptoms of ulcer, the effect on gastric acidity and the incidence of disturbance of gastrointestinal motility as shown by clinical and roentgenologic evidence. All cases in this series were included in the early postoperative studies except for one in which operative death occurred (case 13) which was directly attributable to mediastinitis following a perforation of the esophagus in an attempt to isolate the vagi subdiaphragmatically. The vagi were found at autopsy to be deeply embedded in the esophageal musculature.

*A. Subjective Results.*—In the remaining 41 cases there was a rather striking subjective result. Relief of pain was obtained in all cases except 2, and in all fairness to the procedure it should be stated that both of these patients had overt psychoneurosis, which made subjective evaluation difficult, particularly in view of the fact that they were among the few in whom definite roentgen evidence of healing of the ulcer was apparent. Twenty-two, or 52 per cent, of the patients

had a benign postoperative course, with no immediately recognizable evidence of gastrointestinal atonia, sphincter achalasia or diarrhea and no subjective complaints. These patients were able to leave the hospital completely asymptomatic and on an unrestricted diet.

The remaining 48 per cent of the cases were complicated by troublesome symptoms of impaired gastric motility or other immediate untoward complications.

In addition to severe symptoms of gastric atonia as complications in 2 cases, dysphagia with roentgenologic evidence of esophageal achalasia occurred in 2 patients in conjunction with gastric atonia and was troublesome for two and four weeks respectively. Other complications included persistent diarrhea lasting for two months with spontaneous remission in 1 case. Intestinal obstruction secondary to previous operative adhesions occurred in another case, necessitating a second laparotomy, after which further convalescence was uneventful. Paralytic ileus complicated still another case but responded well to conservative treatment. Other complications, not necessarily related to vagus resection per se, included postoperative abscess of the lung in 1 case, atelectasis in 1 case and severe chemical imbalance consisting essentially of severe alkalosis and hypochloremia, probably secondary to prolonged gastric suction without adequate chloride replacement, in another case.

At the time of the patients' discharge from the hospital, 5 cases in the entire series could be interpreted as showing a poor subjective result. The patients involved included the 2 previously mentioned who did not experience relief of pain, 2 others in whom troublesome symptoms of impaired gastric motility persisted and another patient in whom one vagus nerve was definitely known not to have been severed and whose subjective relief was equivocal. These 5 cases plus the operative death constitute a subjective failure of 15 per cent for the entire series. This is in agreement with an incidence of good subjective results in 87 per cent of a series of 75 patients reported by Moore.<sup>2</sup> The remaining patients all left the hospital on an unrestricted diet and with no symptoms referable to their ulcer.

*B. Studies of Gastric Acidity.*—Studies of gastric acidity in these patients bear out the results of other observers (Moore and others and Grimson and his associates<sup>3</sup>) in that gastric acidity was significantly

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2. Moore, F. D.: Resection of the Vagus Nerves for Ulcer: An Interim Evaluation, *Arch. Surg.* **55**:164-174 (Aug.) 1947.

3. Moore, F. D.; Chapman, W. P.; Schulz, M. D., and Jones, C. M.: Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, *New England J. Med.* **234**:241-251, 1946; Vagus Resection in Peptic Ulcer: Physiologic Effects and Clinical Results, *J. A. M. A.* **133**:741-759 (March 15) 1947. Grimson, K. S.; Baylin, G. J.; Taylor, H. M.; Hesser, F. H., and Rundles, R. W.: Transthoracic Vagotomy: The Effects in Fifty-Seven Patients with Peptic Ulcer and the Clinical Limitations, *ibid.* **134**:925-932 (July 12) 1947.

reduced after vagus resection. Studies of the night secretion and the response to histamine and insulin-induced hypoglycemia were done in the majority of cases. The mean results of these studies as expressed in maximum degrees of free acid is illustrated in table 2. Interestingly, we have found in our preoperative studies of gastric acidity that the patients with a history of perforation have almost consistently had the highest amounts of night secretion and the highest degree of acidity as well as a more marked response to insulin-induced hypoglycemia. This observation deserves further study as it may indicate a possible relationship between the degree of gastric acidity and the tendency to perforation.

It is readily noted that a decided reduction in the response to insulin-induced hypoglycemia is the most striking feature following vagus resection, with a drop of 83 per cent in the maximum acid

TABLE 2.—*Preoperative and Postoperative Gastric Acidity Following Resection of Vagus Nerve*

Operation	Number of Cases Studied	Preoperative			Postoperative		
		Histamine (Maximum Degrees of Free Acid, Mean Values)	Insulin (Maximum Degrees of Free Acid, Mean Values)	Night Secretion, Amount/Degree Acidity (Mean Values)	Histamine (Maximum Degrees of Free Acid, Mean Values)	Insulin (Maximum Degrees of Free Acid, Mean Values)	Night Secretion, Amount/Degree Acidity (Mean Values)
Vagotomy only for duodenal ulcer	12	66.6	83.7	700/20	51	13	247/10.5
Vagotomy for stomal ulcer. ....	8	35	61	815/9	10	7.5	350/9
Vagotomy plus resection or anastomosis. ....	19	52.4	61	777/37	45	13.8	330/2
Totals ..	39	52.3	69.5	764/22	35.3	11.4	376/7

response, from 69.5 degrees preoperatively to 11.4 degrees postoperatively, representing the mean values for the entire series. There is also noted an approximate 50 per cent reduction in the night secretion, whereas the histamine response is the least altered by comparison, with a reduction of approximately 30 per cent. This is at variance with the findings of Crandell and others<sup>4</sup> and of Thornton, Storer and Dragstedt,<sup>5</sup> who found no reduction in acidity with histamine stimulation after transthoracic resection of the vagus nerves. There is no significant difference in reduction of gastric acidity in cases in which resection or gastroenterostomy had been carried out prior to or at the time of vagotomy as compared with cases in which simple vagotomy was per-

4. Crandell, W. B.; Boehm, W. E., and Mulholland, J. H.: Effects of Supradiaphragmatic Section of the Vagus Nerves in Man, *Arch. Surg.* **55**:343-348 (Sept.) 1947.

5. Thornton, T. F., Jr.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of the Vagus Nerves: Effect on Gastric Secretion and Motility in Patients with Peptic Ulcer, *J. A. M. A.* **130**:764-771 (March 23) 1946.



formed. Twenty-one patients in the entire series showed a complete absence of free acid in fasting specimens postoperatively.

Individually considered, however, there was only 1 patient in whom failure to obtain a significant reduction in night secretion and/or insulin response was encountered. He, however, had undergone a simultaneous gastroenterostomy, and the excellent clinical response obtained may have been due entirely to the latter procedure. Similarly, in 4 cases in which one or both vagi were not obtained, as evidenced by failure to find nerve tissue by histologic study in the excised specimens, the studies of postoperative acidity showed a satisfactory reduction. However, all 4 of the patients had undergone simultaneous gastroenterostomy or gastric resection, which indicates what is obviously true, namely, that proper evaluation of vagus resection cannot be made when simultaneous complementary procedures are done which in themselves may cause lowered gastric acidity and relief of symptoms of ulcer.

*C. Roentgenologic Studies.*—Evidence of gastric retention as shown by considerable gastric residue of barium after six hours was shown in

TABLE 3.—*Roentgenologic Evidence of Gastric Retention (Early Postoperative)*

	Number of Cases Studied	Evidence of Retention After 6 Hours	Incidence, Percentage
Vagotomy alone.....	9	7	78
Vagotomy for marginal ulcer.....	6	2	33
Vagotomy plus resection or anastomosis	9	3	33
Totals.....	24	12	50

48 per cent of 24 patients who were given postoperative roentgenologic examinations. Roentgenologic studies were otherwise generally inconclusive, since most of the patients who showed duodenal deformity preoperatively showed roentgen evidence of continued deformity postoperatively. What could be interpreted as healing of the ulcer in the roentgenogram occurred in 8 cases. It is obvious, of course, that the interpretation of healing roentgenologically must of necessity eliminate the cases in which complementary gastrectomy was done and that the duodenal ulcer will probably not be visualized in most of the cases in which complementary gastroenterostomy was performed. There remain only 12 cases in which preoperative and postoperative roentgen studies were available. Of the 12 patients, 7, or 58.3 per cent, showed evidence of actual disappearance of an active ulcer crater, although deformity persisted. These included 3 patients with duodenal ulcer and 3 with stomal ulcer. In the patient with gastric ulcer there was complete healing on roentgen study two weeks postoperatively.

Table 3 indicates the roentgenologic incidence of gastric retention as evidenced by residual barium in the stomach estimated at 25 per cent

or over after six hours. In 24 cases in which postoperative roentgenograms were made the total incidence of this complication was 50 per cent. With vagotomy alone, evidence of retention was observed in 7 of 9 cases, or 78 per cent.

#### FOLLOW-UP STUDIES

In order to valuate the procedure in the light of late results, all patients for whom at least three months had elapsed since operation were requested to return to the hospital for examination or to reply to a questionnaire relative to their symptoms. We were thus able to study

TABLE 4.—*Roentgenologic Studies in Cases of Vagotomy Only*

Case	Early Postoperative	Months Since Operation	Follow-Up
1	Large gastric residue after 24 hours	10	70 per cent retention after 24 hours; possible prepyloric ulcer
5	Duodenal ulcer deformity and crater with 25 per cent retention after 6 hours	11	Old duodenal ulcer deformity with 30 per cent retention at 6 hours
6	Esophageal achalasia and 25 per cent gastric retention after 6 hours	6	Dilated stomach with 50 per cent residual after 6 hours
7	Duodenal ulcer deformity with disappearance of crater; 50 per cent gastric retention after 6 hours	11	65 per cent retention at 30 hours; stomach empty at 48 hours
11	Duodenal deformity; almost complete gastric retention at 6 hours	10	70 per cent retention at 24 hours; stomach empty in 48 hours
14	Duodenal scarring, 40 per cent gastric retention at 6 hours; esophageal achalasia	9	40 per cent gastric retention after 24 hours
38	.....	3	40 per cent gastric retention after 24 hours
12	Gastric ulcer healed within 2 weeks; no disturbance of motility	..	.....
21	50 per cent retention	3	No retention
29	Ulcer healed by roentgenogram; no retention	3	No retention

a total of 25 patients at intervals varying from three to twelve months after operation. These included 10 of the 12 patients in whom resection of the vagus nerve only was done, 11 of the 20 patients who underwent such resection plus a complementary procedure and 5 of the 10 patients operated on for marginal ulcer.

*A. Vagotomy Only.*—In this group we were able to obtain roentgenologic studies on 9 patients, as shown in table 4. It is readily noted that only 2 of the patients who had shown evidence of early postoperative gastric retention showed no retention in the follow-up studies (cases 14 and 21). Six patients showed either a persistence of retention or even more pronounced evidence of it than was observed on their early postoperative roentgenograms, 4 of them failing to show com-

plete gastric emptying after twenty-four hours and 3 of these showing retained barium estimated at 70 per cent or over. These studies indicate a late incidence of gastric retention of 78 per cent from three to eleven months after operation, which is identical with the early postoperative incidence after vagotomy alone as noted in table 3. Table 5 summarizes the follow-up roentgen evidence of gastric retention for the entire series.

Follow-up studies of gastric acidity were obtained after simple vagotomy in 6 of these patients who consented to return to the hospital for such studies. A comparison of the mean values for gastric acidity in the early and the late postoperative studies is indicated in table 6.

It is seen that the night secretion remained constant, although there is a small rise in the mean response to insulin in the later post-

TABLE 5.—Late Postoperative Roentgenologic Evidence of Gastric Retention

	Number of Cases Studied	Evidence of Retention After 6 Hours	Incidence, Percentage
Vagotomy alone.....	9	7	78
Vagotomy for marginal ulcer.....	4	1 (slight)	25 (?)
Vagotomy plus resection.....	3	0	0
Vagotomy plus gastroenterostomy.....	5	3	60
Totals.....	21	11	52

TABLE 6.—Gastric Acidity

	Number of Cases	Histamine (Maximum Degrees of Free Acid)	Insulin (Maximum Degrees of Free Acid)	Night Secretion, Cc./Degree
Early postoperative studies.....	12	51	13	247/10.5
Late postoperative studies.....	6	30	22.5	241/10.8

operative studies. Although this rise is probably too small to be of great significance at the present time, it is of interest in the light of experimental resection of the vagus nerve in dogs in which it has been shown by Vanzant<sup>6</sup> that gastric acidity will return to preoperative levels in about two years.

Subjective follow-up studies were obtained in 10 of the 12 cases with regard to symptomatic results. One of the patients who had undergone a transthoracic vagus resection for treatment of a supposed duodenal ulcer on Dec. 19, 1946, with apparently good symptomatic relief on discharge, died eight months later at another hospital. A diagnosis of carcinoma of the stomach with metastasis was made at

6. Vanzant, cited by Walters, W.; Neibling, H. A.; Bradley, W. F.; Small, J. T., and Wilson, J. W.: Gastric Neurectomy: Anatomic and Physiologic Studies with Favorable and Unfavorable Results in the Treatment of Peptic Ulcer, Arch. Surg. 55:151-163 (Aug.) 1947.

autopsy. It is obvious that this lesion must have existed at the time of his original operation, and this gives added strength to the contention that an abdominal approach, with direct visualization of the lesion, is preferable to the transthoracic approach (Walters and others,<sup>7</sup> Grimson and his associates<sup>8</sup>). Bradley and others<sup>9</sup> concluded that a sub-diaphragmatic approach would allow nearly as complete a division of all the gastric nerves as a transthoracic approach in over 90 per cent of cases.

The remaining 9 patients all stated that they had had continued relief from pain. Pronounced symptoms referable to gastric atonia were present in 3 patients ten months postoperatively, consisting of postprandial belching, foul breath and postprandial fulness and/or distention. In spite of these symptoms, 1 patient had gained 18 pounds (8.2 Kg.) in weight and another 8 pounds (3.6 Kg.), and the weight of the third had remained stationary. Two of these 3 patients are dissatisfied with their result. Both of these patients had poor subjective results in the early postoperative period also. Urecholine<sup>®</sup> (carbominoyl-beta-methylcholine chloride) administered to each of these patients as described by Machella, Hodges and Lorber<sup>10</sup> was without clinical effect on gastric emptying. The remainder of the patients who showed roentgen evidence of gastric retention reported no troublesome symptoms of major importance relative to this finding, and all felt that they had been benefited by the operation.

Only 3 of the patients failed to report a gain in weight. One of these had a moderate diarrhea, which developed two months postoperatively and has persisted for seven months. No other cases of troublesome diarrhea were reported. A definite history of hemorrhage was obtained in only 1 patient, who stated that he had had several tarry stools since operation and was readmitted to the hospital with a severe hemorrhage eleven months after surgical intervention.

A summary of the subjective results is shown in table 7. It is noted that although 78 per cent of patients showed considerable roentgen evidence of gastric atonia ten months after vagotomy the symptoms of this complication were severe enough to be troublesome in only 33

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7. Walters, W.; Neibling, H. A.; Bradley, W. F.; Small, J. T., and Wilson, J. W.: Gastric Neurectomy for Gastric and Duodenal Ulceration: An Anatomic and Clinical Study, *Ann. Surg.* **126**:1-18, 1947. Vanzant.<sup>6</sup>

8. Grimson, K. S.; Baylin, G. J.; Taylor, H. M.; Hesser, F. H., and Rundles, R. W.: Clinical Evaluation of Complications Observed After Transthoracic Vagotomy, *Arch. Surg.* **55**:175-179 (Aug.) 1947.

9. Bradley, W. F.; Small, J. T.; Wilson, J. W., and Walters, W.: Anatomic Considerations of Gastric Neurectomy, *J. A. M. A.* **133**:459-461 (Feb. 15) 1947.

10. Machella, T. E.; Hodges, H. H., and Lorber, S. H.: The Restoration of Gastric Motility by Urethane or B-Methyl Choline After Section of the Vagus Nerves for Peptic Ulcer, *Gastroenterology* **8**:36-51, 1947.

per cent. Our studies thus tend to corroborate the statement of Walters and others<sup>6</sup> that "the results are inconstant, variable and in most cases unpredictable."

*B. Vagotomy Plus Complementary Gastric Operation.*—Additional follow-up studies were also obtained on 11 patients who were subjected to gastroenterostomy or partial gastrectomy performed simultaneously with vagus resection.

All the patients from whom a history could be obtained reported notable subjective improvement without exception. Annoying subjective symptoms which might be attributable to gastric atonia were not present in any of the cases. There was no history of hematemesis or melena. Most of the patients were enthusiastic about their symptomatic

TABLE 7.—*Symptomatic Evaluation of Simple Vagotomy  
Three to Twelve Months After Operation*

Case	Relief of Pain	Symptoms of Gastric Atonia	Hemorrhage	Diarrhea	Change in Weight, Lb.	Evaluation by Patient	Months Since Operation
1	Complete	Severe	None	None	+18	Good	11
5	Complete	Mild belching and slight fullness	2 to 3 tarry stools; severe hemorrhage	None	+ 5	Good	11
7	Partial	Severe	Equivocal	Mild	+ 8	Poor	11
11	Partial	Severe	None	5 times daily	No change	Poor	10
14	Complete	None	None	None	+30	Excellent	9
12	Complete	None	None	None	+15	Excellent	10 Gastric ulcer
21	Complete	Mild	None	Severe	-15	Good	7
29	Complete	Mild	None	3 times daily	-10	Good	7
38	Complete	Mild	None	None	+ 1	Excellent	3

result. One patient in whom the right vagus had not been found at his original operation and who had continued to complain of pain in spite of an early postoperative reduction in gastric acidity underwent a lobectomy six months later for abscess of the lung, at which time the right vagus nerve was divided in the chest. This procedure was followed by relief of pain, and the patient was subsequently discharged symptom free. All the patients except 1 had gained weight.

Studies of gastric acidity were made on only 4 of these patients, 2 of whom had undergone gastroenterostomy and 2 with gastric resection. Both of the former showed no significant change in acid values in a three and six month interval, respectively. Interestingly, both patients in whom gastric resection had been done showed a complete absence of free acid in response to both histamine and insulin. Follow-up roentgenologic studies on 5 patients who had undergone gastroenterostomy revealed evidence of gastric atonia in 3. The retention was of consid-

erable degree, with 60 per cent in seven hours and incomplete emptying in twenty-four hours in 1 case seven months after operation, 75 per cent retention after six hours in another case six months postoperatively and 40 per cent retention three months postoperatively in the third case. Three patients studied who underwent vagotomy plus gastric resection showed no roentgenologic evidence of gastric retention. This indicates an incidence of 60 per cent gastric retention in spite of gastroenterostomy performed simultaneously with vagotomy as compared with an incidence of 78 per cent in patients treated by means of vagotomy alone (table 5). These figures coincide with the early postoperative figures and indicate that the disturbance of gastric motility is not as temporary as has been stated by some observers.

*C. Vagotomy for Marginal Ulcer.*—Of the 4 patients treated for marginal ulcer on whom we were able to obtain follow-up studies, all claimed an excellent symptomatic result. Of the 4 patients who were studied roentgenologically, 1 showed slight retention of barium after ten hours. In only 2 of these patients were studies of gastric acidity repeated. In 1 case there was a return to the preoperative level with the use of histamine and a rise of 25 degrees with the use of insulin five months after surgical intervention. In the second patient the histamine response exceeded the preoperative level, although the insulin response was unchanged.

#### COMMENT

Our findings thus far indicate a good subjective result in 85 per cent of the patients in this series, although 3 of 10 patients (30 per cent) who underwent vagotomy alone had severe symptoms related to gastric atonia as long as ten months postoperatively. The degree of subjective improvement is more striking and the incidence of complications reduced when complementary gastroenterostomy or gastric resection is done. Although there are too few cases to be conclusive, it seems that our best results were obtained in cases in which vagotomy was combined with gastric resection.

Roentgenologic studies revealed that over 75 per cent of patients who underwent vagotomy alone showed decided evidence of gastric retention. With complementary gastroenterostomy, gastric retention was present in over 50 per cent of cases, and with complementary gastric resection this complication was negligible. Roentgenologic studies repeated from three to twelve months postoperatively showed no reduction in the incidence of impaired gastric motility. The operation definitely produces a reduction in gastric acidity which is most noticeable (83 per cent) in the response to insulin-induced hypoglycemia, with a lesser reduction (50 per cent) in the night secretion and relatively little reduction (30 per cent) in the response to histamine.

Follow-up studies of gastric acidity as long as eleven months post-operatively indicated a slight rise in the response to insulin, with relatively little change in the night secretion or the histamine response. There has been no evidence of recurrent ulceration in this series thus far except in the case in which massive hemorrhage occurred ten months after vagotomy.

Since the follow-up period in this series of cases does not exceed twelve months, it seems that further studies are indicated at subsequent intervals before definite conclusions can be drawn as to the relative merit of vagotomy compared with present standardized surgical methods of treatment for peptic ulcer.

The results of vagotomy as thus far reported in the literature are not as consistently good as those reported for conventional gastric resection by Wangenstein,<sup>11</sup> Walters, Gray, Priestley and Counseller<sup>12</sup> and others. This study further substantiates these reports. It should be recalled, also, that the results thus far reported are no better than those reported during the years when gastroenterostomy alone was considered the surgical treatment of choice for peptic ulcer (Balfour<sup>13</sup>). It will be of interest to note the effect of vagotomy on the incidence of marginal ulcer over a long period in cases in which combined procedures have been done.

#### SUMMARY

1. Forty-two cases of peptic ulcer treated by resection of the vagus nerve are reviewed from the standpoint of early and late clinical results.
2. Two deaths are reported, one due to esophageal perforation at operation and the other due to gastric carcinoma unrecognized because of a transthoracic approach.
3. Early and late results are compared from the standpoint of subjective results and of effects on gastric acidity and on gastric motility.
4. The results of vagotomy in this series were best when this procedure was combined with gastric resection.
5. As a whole, the data in this series indicate that the results so far are not consistently as good after vagotomy as after conventional gastric resection.

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11. Wangenstein, O. H.: The Role of the Surgeon in the Management of Peptic Ulcer, *New England J. Med.* **236**:191-196, 1947.

12. Walters, W.; Gray, H. K.; Priestley, J. T., and Counseller, V. S.: Annual Report on Surgery of the Stomach and Duodenum for 1942, *Proc. Staff Meet., Mayo Clin.* **18**:505-511, 1943.

13. Balfour, D. C.: Results of Gastro-Enterostomy for Ulcer of the Duodenum and Stomach, *Ann. Surg.* **92**:558-562, 1930.

# INTRAVENOUS ADMINISTRATION OF PROCAINE HYDROCHLORIDE FOR PAINFUL PROLAPSED HEMORRHOIDS

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**P**ROLAPSED hemorrhoids are usually excruciatingly painful, yet unless strangulation ensues most surgeons prefer not to operate until the marked edema has subsided. During this period of waiting, which may last several weeks, the discomfort is often extreme. Although some relief may be afforded by putting the patient to bed, administering narcotics and applying heat or analgesic ointments locally, the severe pain frequently persists, and locomotion becomes difficult. To relieve the sufferings of these unhappy persons, a 1:1,000 solution of procaine hydrochloride was injected intravenously. This is a report of our experience with that method of treatment.

All the patients studied were men admitted for the treatment of severe pain in the anal region. Two types of pain appeared to be present—a sharp radiating pain and a dull pain localized in the anal region but increased by motion of the thighs. All the patients exhibited prolapsed hemorrhoids associated with edema and often ulceration of the anal mucosa; a few showed beginning strangulation. These patients had been treated, without relief, with the usually recommended procedures, some of which have been mentioned.

After a preliminary period of observation, some of the patients received a 1:1,000 solution of procaine hydrochloride intravenously in a volume containing 4 mg. per kilogram of body weight.<sup>1</sup> The predetermined dose was injected in exactly twenty minutes. Another group received 1 Gm. of procaine hydrochloride in a liter of isotonic

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1. Graubard, D. J., and Ritter, H. H.: Intravenous Procaine in the Treatment of Trauma, *Am. J. Surg.* **74**:765-769 (Nov.) 1947.



sodium chloride solution injected intravenously over a three to four hour period. The first method is suitable for the home and office and the second for the hospital. No barbiturates or narcotics were administered. To aid in reducing the anal edema, the patients were requested to stay in bed but were allowed bathroom privileges. During the period of this study only one intravenous injection of the procaine solution was given daily. The daily injections were continued until pain was markedly relieved. Usually no treatment was required after the third day.

The first injection was often accompanied with a sensation of warmth in the face or extremities; some patients occasionally complained of feeling faint. Succeeding treatments usually produced no significant reactions. In our experience with over four hundred injections no serious accidents have occurred.

The results of treatment are as follows: A definite reduction of the "sharp" pain occurred within three minutes after the first intravenous injection was started. The dull localized pain subsided shortly thereafter. Complete comfort persisted for five to ten hours after the twenty minute method and for seven to twelve hours after the longer procedure. Partial relief for the remainder of the day followed with both methods. Some rectal discomfort was present the next morning, but on repetition of the treatment it abated in a similar manner. If pain then recurred, it did so with diminished fury. The procaine hydrochloride was usually needed through the third day; thereafter, many patients were comfortable and required no further medication. It was noted that ulceration, if present, frequently healed by the fifth day. The treatment may have diminished the duration of the edema, but this was difficult to evaluate without a large series of controls. Some hemorrhoids still protruded several days after cessation of treatment, but, peculiarly enough, they no longer gave rise to severe symptoms.

The results of treatment have been almost identical in all our cases. Three representative histories are given to demonstrate the effect of intravenous administration of procaine hydrochloride.

CASE 1.—A 48 year old Negro was admitted to the hospital with a history of having his "whole rectum" protrude suddenly six days previously. He complained of severe anal pain and weakness. On examination, internal hemorrhoids were found prolapsing through a tight sphincter; there was marked edema, and an area of necrosis in the rectal mucosa measured 1.5 cm. in diameter.

At noon on Jan. 29, 1948, a grain (60 mg.) of codeine was given subcutaneously, without relief; the prolapsed hemorrhoids were extremely painful. At 1:45 p. m., injection of a 1:1,000 solution of procaine hydrochloride was started, and the pain was relieved four minutes later. At 2:05 p. m. 300 cc. of the solution had been given and the intravenous injection was discontinued. The patient was able

to walk about without pain for the first time since the onset of his illness. Pain returned at 5:30 p. m. but disappeared spontaneously at 8 p. m.

On January 30 the patient felt better but still had anal pain and edema. A 1:1,000 solution of procaine hydrochloride in isotonic sodium chloride solution was injected intravenously. This was discontinued after 300 cc. had been given in exactly twenty minutes. The anal discomfort was completely relieved.

On January 31 the ulceration of the rectal mucosa appeared to be unchanged. The edema of the prolapsed structures had diminished about 50 per cent, and little rectal pain was present. Although the edema appeared to be slight, pain had recurred in the anal region by February 4. The patient was given 300 cc. of procaine hydrochloride as before in exactly twenty minutes, beginning at 8:25 a. m. At 2:15 p. m. he had a bowel movement without pain, but he noticed a burning sensation during defecation.

On February 5 the ulceration of the rectal mucosa appeared to be healed. No pain was present. The patient was discharged on February 9 with his ulcer healed, the edema gone and the prolapse of his internal hemorrhoids no longer present.

CASE 2.—A 38 year old white man was admitted with a history of having had hemorrhoids since February 1945. On various occasions they had "dropped out," remaining out for several days and causing severe pain and bleeding. Four days prior to his admission the hemorrhoids had again "dropped out," and the patient was unable to reduce them. The pain was so severe that he was admitted for emergency treatment.

On examination, large prolapsed internal hemorrhoids were found. One of them appeared to be thrombosed. Although considerable edema was present, there was no ulceration of the prolapsed mucosa.

On March 24, 1948, beginning at 8:25 p. m., the patient was given 1 Gm. of procaine hydrochloride dissolved in 1 liter of isotonic sodium chloride solution. The solution was given over a three hour period. During the injection the patient fell asleep and slept well all night. At noon on March 25 the same injection was repeated. The patient had no reaction and felt comfortable. At 7 p. m. he was up and about the ward. On March 26 the extent of the prolapse appeared to be diminished. At 10 a. m. a liter of 1:1,000 solution of procaine hydrochloride was given. The patient had no pain during the remainder of the day but did complain of some soreness during defecation.

On March 27 the injection was repeated. The edema was decreasing, and little pain was present. The pain disappeared completely after the beginning of injection of procaine. The patient still had some soreness during defecation, however. On March 31 the prolapse was completely reduced. Rectal examination revealed a tight sphincter, but the examining finger could be passed through it.

On April 1 a hemorrhoidectomy was performed. Moderate edema of the external hemorrhoids was noted during the operation.

CASE 3.—A 50 year old Negro was admitted for the treatment of severe anal pain. Hemorrhoids had been present for the past ten years, but five days prior to his admission they had prolapsed.

On examination, prolapsed internal hemorrhoids were found associated with ulceration of the prolapsed mucosa. The ulcer measured 1 cm. in diameter. A severe grade of edema of the prolapsed structures was also noted.

On March 11, 1948, the patient complained of severe anal pain. At 9:15 a. m. injection of a 1:1,000 solution of procaine hydrochloride in isotonic sodium chloride

solution was started. At 9:18 a. m. the "shooting" pain was gone; soreness on motion was present in the anal area. At 9:20 a. m. there was less soreness on motion, and no toxic symptoms were noted. At 9:25 a. m. the patient began to feel "funny." This seemed to be caused by a sensation of warmth all over the body. At 9:28 a. m. the "funny" sensation had disappeared. At 9:35 a. m. the intravenous injection was discontinued after 300 cc. had been given. No pain was present at this time.

On March 12 there was some pain in the anal region, but this appeared to be milder than on the previous day. Three hundred cubic centimeters of a 1:1,000 solution of procaine hydrochloride in dextrose was injected intravenously; no reaction occurred. On March 13 the edema of the prolapsed structures had diminished about 25 per cent, and the ulceration had decreased in size. There was much less pain, but soreness on motion persisted. The procaine solution was again injected intravenously.

On March 15 there was no pain. Some prolapsed hemorrhoids were present on the left; those on the right appeared to have reduced. On March 17 the ulceration of the prolapsed rectal mucosa had healed. The patient felt comfortable.

On March 18 the patient was up all morning. At noon the hemorrhoids again prolapsed; attempts at reduction failed. He was treated with narcotics and Sitz baths, without relief. The injection of procaine solution was repeated at 3:15 p. m., with complete relief of pain. Three hundred cubic centimeters was given in exactly twenty minutes. No pain was present on March 19. By March 29 pain was still absent. The hemorrhoids were ready for operation since March 20, but the patient was watched for the purpose of this study. There appeared to be some rectal mucosa everting through the relaxed anal sphincter. On April 1 a modified Whitehead type of operation was done.

#### COMMENT

There are various factors accounting for the success of this method of treatment. The nerve supply of the veins is similar to that of the arteries since both show nerves ending in the adventitia and the media. Some claim to have demonstrated nerve endings in the intima. One would therefore expect to find relief of pain in a disease of the veins, such as prolapsed hemorrhoids, by a direct action of the anesthetic solution on the nerve endings.<sup>2</sup> In addition, there is evidence suggesting that procaine hydrochloride diffuses easily through the vessels showing increased permeability because of disease. It has been demonstrated that after trauma the concentration of procaine hydrochloride in the traumatized area is seven to eight times that in the blood.<sup>1</sup> When the hemorrhoids are prolapsed or strangulated, there is notable edema of the structures, and it is likely that the solution diffuses into the edematous areas and there exerts its well known anesthetic effect, which relieves the dull localized type of pain and the pain increased by motion of the thighs. It is probable that the

2. De Sousa Pereira, A.: The Innervation of the Veins, *Surgery* 19:731-742 (May) 1946.

condition of prolapse or strangulation of the hemorrhoids sets up a reflex vasospasm and sphincter spasm which causes the sharp shooting pains. This reflex vasospasm has been demonstrated in thrombophlebitis of the lower extremities. The procaine hydrochloride acting on the nerves in the prolapsed hemorrhoids blocks the starting point of the reflex, thus relieving the reflex vasospasm and the sphincter spasm. Relief of sphincter spasm is suggested by the fact that several days after treatment is discontinued protruding hemorrhoids, although still present, are relatively painless. Relief of the reflex vasospasm may account for the rapid healing of the ulcers in the protruded mucosa.

#### SUMMARY

A solution of procaine hydrochloride injected intravenously in recommended doses gave prompt and considerable relief of pain in 3 patients with prolapsed hemorrhoids.

## TREATMENT OF CANCER OF BREAST BY SIMPLE MASTECTOMY AND ROENTGENOTHERAPY

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CANCER of the breast is one of the commonest forms of malignant disease in women. If it is fully treated when still localized, many lives may be saved. The maximum number of lives will be saved by the use of the most effective methods of treatment. So that these may be recognized it is essential that a reliable means of assessment be employed.

The very fact that there is still great doubt regarding which method is best suggests that the usual methods of assessment are not reliable. To continue to publish unreliable assessments will only further confuse the issue; much time and energy will be wasted, and many lives may be lost.

Some of the present confusion undoubtedly arises from the failure to appreciate that the value of a method of treatment depends not on the results obtained in the treated patients but on the number of lives a method may save. Thus if a method is suitable for only a limited number of cases it cannot be regarded as a good method even though the results obtained in the few selected cases may be good.

There is no more certain method of securing good results than by careful selection of patients for treatment, but by restricting a method to only the most favorable cases some lives may be lost that might otherwise be saved. It must rarely happen, however, that lives will actually be sacrificed so that good results will be obtained, but it is not uncommon to limit the use of a method to early cases and to apply some alternative method in the more advanced cases. Thus as the limitations of radical mastectomy become more clearly recognized, it has become customary to restrict the operation to early cases and to refer all the more advanced cases for treatment by roentgenotherapy. If only treated patients are considered, the results from radical mastectomy in these circumstances will appear to be good.

There is little doubt that the improved results now being recorded for radical mastectomy are due to more careful selection, but the care taken in the selection of patients varies greatly from surgeon to surgeon, and the variation in the results presented is almost certainly due more to this variation in selection than to any difference in operative skill.

It is of course desirable that some selection should take place, for to operate in advanced cases may not only shorten life but may in addition increase the terminal discomfort of the patient.

From what has been said it will be obvious that when two methods of treatment are being compared an entirely erroneous conclusion may be reached if the comparison is based entirely on the patients actually treated. It cannot be too strongly emphasized that the true value of a method of treatment depends just as much on the number of cases to which it will apply as on the results obtained when it is applied. In order to avoid the distorting influence of selection the fact must be accepted that the only really reliable survival rates are those obtained by expressing the number of survivors as a percentage of the total cases referred. No case must be omitted from the total for any reason whatsoever.

It is agreed that the proportion of advanced cases may vary from one hospital to another, but it is difficult to see how proper allowance can be made for this. A common method of attempting to overcome this difficulty is to make use of one of the many systems of staging. None of the methods of staging so far devised is free from variation in interpretation. The following example will show the dangers of comparing the value of two methods of treatment on this basis.

*Two Identical Series of Patients Treated by Methods of Equal Value*

	Stage I	Stage II
Series A	Early cases	Advanced cases
Series B	Early cases	Advanced cases

Owing to a difference in interpretation, the cases in stage I of series A have been more carefully selected than the cases in stage I of series B. In consequence, in stage I series A there will be fewer moderately advanced cases than in stage I series B. The results in stage I series A will therefore be higher. In stage II series A the results will also be higher because there will be more cases in which the disease is only moderately advanced than in stage II series B. Comparison by stages might suggest that the method used in series A

was better than that used in series B. It should be noted that the survival rates will be the same when the total number of survivors is expressed as a percentage of the total number of patients.

The same findings will be obtained when the subdivision extends to more than two groups. For the same reasons it is equally dangerous to compare the value of two methods of treatment by a division of cases into operable and inoperable groups.

A fuller account of the influence of selection has been given elsewhere,<sup>1</sup> but the following brief summary will provide some indication of the essential points which must be observed when methods of treatment are being compared.

1. When the value of any method or combination of methods is being assessed no case must be deducted from the total. Cases in which treatment was not completed and cases in which the method cannot be applied are just as much failures as those in which full treatment was given and the patient failed to be cured.

2. The only reliable results are those of a large general hospital where records are made of all patients coming to the hospital irrespective of whether they are admitted or not.

3. The limitations of any method of staging—clinical, histologic or a combination of the two—must be recognized, and while results may be presented by stages the figure of greatest value is the survival rate for all the stages taken together. This figure should always be stated.

4. When the proportion of untraced patients is high, it is best to express the survival rate as lying between two percentages. These two percentages are obtained by assuming, on the one hand, that all untraced patients are alive and, on the other, that they are all dead.

5. While deaths from intercurrent disease may be deducted, the death rate from these causes should not exceed that for the corresponding age group of the population as a whole.

6. "Clinical cure rates" and "symptoms free rates" are too unreliable to be of value. Even when the assessment is made at the clinic there may be considerable doubt as to whether the patient is free from disease or not, and when the assessment is made by the patient or by the family physician, it is, as a rule, so unreliable as to be of limited value. The "clinical cure rate" must always remain a statement of opinion and, therefore, less reliable than the survival rate, which is a statement of fact.

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1. McWhirter, R.: The Value of Simple Mastectomy and Radiotherapy in the Treatment of Cancer of the Breast, *Brit. J. Radiol.* **21**:252 (Dec.) 1948.

The adoption of this basis of assessment will provide results which may come as a great disappointment to those who in the past have been content to calculate the survival rates of only those patients who were fully treated.

Thus while five year survival rates varying (according to the degree of selection) from 35 to 45 per cent may be obtained for patients actually treated by radical mastectomy, I do not believe that the five year survival rate will exceed 25 per cent when all cases referred to a large general hospital are included in the total on which the survival rate is based.

Put in another way, the radical operation fails in approximately 75 per cent of cases as judged by the five year survival rate. It was because radical mastectomy was recognized to fail in so many cases that it was decided in Edinburgh to explore the value of other methods of treatment.

The value of combining postoperative roentgenotherapy with radical mastectomy was first investigated. The method was successful in reducing the number of local recurrences, but many patients continued to die from distant metastasis. This led to the belief that dissection of the axilla might cause dissemination of malignant cells to sites beyond the area which could be irradiated. At the time of the operation tissues invaded by the tumor must commonly be divided and the trauma inflicted on involved tissues must increase the natural tendency of malignant cells to be disseminated to distant sites. Should cells be disseminated to distant sites before roentgenotherapy is applied, the latter will not be effective in saving the life of the patient. In an attempt to overcome this difficulty it was decided to continue to remove the breast surgically but that the treatment of the axilla should be by roentgenotherapy alone.

#### FACTORS WHICH SUGGESTED THE USE OF SIMPLE MASTECTOMY AND ROENTGENOTHERAPY

The decision to treat cancer of the breast by this means was taken at a meeting of the surgical staff in 1941. The decision was made for the following reasons.

1. When the disease is confined to the breast, surgical intervention gives good results. Surgical treatment is thus an effective method of treating the disease in the breast, and it was decided that surgical removal should be continued.

2. While at first sight surgical intervention might appear to be the most satisfactory method of treating the axilla, a more careful examination will show that its value is in fact limited. It is true that the results are excellent when the axillary glands are not involved, but if there are



no malignant cells in the axilla it would appear unnecessary to dissect it, for the removal of normal lymph nodes cannot influence the result. On the other hand, when the axilla is secondarily involved, there is universal agreement that radical mastectomy often fails to save the life of the patient. Since, therefore, surgical removal of the glands is unnecessary when the axilla is not involved and often fails when the axilla is involved, it was decided to treat the axilla by roentgenotherapy to see if better results could be obtained.

3. In many forms of cancer roentgenotherapy has now become the treatment of choice, and in carcinoma of the breast it has been shown that postoperative recurrences can be effectively treated by this means. Immediate postoperative roentgenotherapy will greatly reduce the number of local recurrences. From these observations it must be concluded that this therapy can destroy breast cancer cells and that it is at least an alternative method of treating the axilla.

Soon after this method of treatment was introduced it was found that a much higher proportion of patients could be given full treatment than had been possible before. Thus the prospect of cure was offered to a greater number of patients, and, as will be shown later, patients with fixed axillary glands and with glands present in the supraclavicular region were treated with a considerable measure of success.

The wound heals more quickly after the simple mastectomy. Roentgenotherapy can therefore be applied with less delay, and the interval during which cells may escape to distant sites is thus reduced.

When patients are treated by radical mastectomy and roentgenotherapy, edema of the arm is common. With simple mastectomy and roentgenotherapy edema of the arm is almost unknown.

#### DATA FOR YEARS 1941 TO 1945

*Number of Cases.*—In the period 1941 to 1945 the number of cases of cancer of the breast referred to the Royal Infirmary was 1,451, and of this number 1,334 were primary cases. The remaining 117 patients had all been treated elsewhere and were referred only after the development of recurrences.

Each primary case was classified when it was first seen, and the classification adopted was that suggested by Paterson of Manchester.<sup>2</sup> It should be noted that this classification is based entirely on the pre-operative clinical findings.

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2. The Results of Radium and X-Ray Therapy in Malignant Disease: Second Statistical Report from the Holt Radium Institute, Manchester, 1934-1938.

*Operability.*—There are many standards of operability, and, as already indicated, all of them are subject to great variation in interpretation. It is, nevertheless, convenient in the presentation of an account of the results to divide cases into groups.

In a previous communication<sup>3</sup> the condition in stages I, II and III of the classification in table 1 was regarded as operable, but it would appear that this standard is too low. It is now recognized that stage III cases are too advanced for treatment by radical mastectomy, and, in order to conform to modern standards, only stages I and II will now be included in the operable category. The definition of operability will then read as follows:

The primary tumor, which may be of any size, may show any degree of cutaneous involvement up to and including ulceration, but there must be no isolated nodules of the skin or other manifestation

TABLE 1.—*All Primary Cases Referred in the Period 1941 to 1945*

	Stage I	Stage II	Stage III	Stage IV	Total
Number.....	405	344	182	403	1,334
Percentage.....	30	26	14	30	100

TABLE 2.—*Results in Advanced Cases with Respect to Metastases*

1941 to 1945	Operable Cases	Advanced, Without Distant Metastases	Advanced, with Distant Metastases	Total
Number.....	749	387	198	1,334
Percentage.....	56	29	15	100

of invasion of the cutaneous lymphatic vessels. The extent of involvement of the skin must not be so great as to necessitate skin grafting when radical mastectomy is performed, and the tumor must not be fixed to the pectoral muscle. The axillary glands of the same side may be enlarged, but they must not be fixed. The supraclavicular glands must not be enlarged, and there must be no clinical or roentgenologic evidence of more distant metastases.

It will be observed that stage I and stage II cases constitute 56 per cent of the total cases referred. During the period when radical mastectomy was employed it was found that in 60 per cent of the cases in stage I and in 15 per cent of the cases in stage II the axillary glands were not involved on histologic examination. When the two stages are taken together to form the operable group, it may therefore be

3. McWhirter, R.: The Treatment of Cancer of the Breast, Proc. Roy. Soc. Med. 41:122 (Feb.) 1948.

presumed that in 40 per cent of cases the axillary glands will not be histologically involved, while in the remaining 60 per cent the glands will be found to be invaded by malignant cells.

For further convenience in the presentation of the results the advanced cases have been divided into two groups in table 2 according to whether or not distant metastases were present.

*Operative Mortality.*—The operations were performed by upward of forty different surgeons, and, while only 11 postoperative deaths (death within a month from any cause was regarded as a postoperative death) are known to have taken place, it was decided to add another 11 deaths to the total to allow for any possible further postoperative deaths in patients who were operated on outside the Royal Infirmary. These added deaths are almost certainly in excess of the number which actually took place, but as the exact number was unknown it was decided to err on the safe side so as to avoid any criticism that might arise.

Of the 11 known deaths, there were only 4 in patients under 65 years of age. The remaining 7 occurred in elderly debilitated patients.

*Untraced Patients.*—No patient was untraced.

*Histologic Confirmation.*—Of the operable cases, 97 per cent were histologically proved, and among the total there was histologic confirmation in 87 per cent. The cases not histologically proved were mainly those too advanced for any surgical treatment.

*Calculation of Survival Rate.*—The method adopted is that advised by Dr. Lewis-Faning of the Medical Research Council. A full account of the method cannot be given here, but briefly it may be stated that, while the five year survival rate of the patients treated in the period 1941 to 1945 is mainly determined by the patients treated in 1941 and 1942, the rate is influenced by the patients treated in the later years. By allowing the more recently treated patients to influence the five year survival rate, a figure is obtained which is more reliable than that based on the 1941 and 1942 cases alone.

For comparison the five year survival rate calculated by the more usual method is given at the end of table 5. It so happens that there is no great difference between this figure and that obtained by the method adopted. The method advised by Dr. Lewis-Faning, however, has the great advantage that the five year survival rate is based on a much larger number of cases and is therefore to be preferred.

#### SURVIVAL RATE FOR ALL OPERABLE CASES IN THE PERIOD 1941 TO 1945

As has been stated the main method of treatment in this period was simple mastectomy and roentgenotherapy. Full treatment was possible in almost all cases, but whether this was given or not, every case classified as operable has been included in table 3.

As will be observed from the last column the five year survival rate is 62.1 per cent.

During the period 1935 to 1940, the main method of treatment was radical operation and postoperative roentgenotherapy, and of the 411 patients whose condition was operable, 50.1 per cent were alive at the end of five years.

Statistical examination shows that this difference in the survival rates is significant, and the findings, so far as the five year survival rate is concerned, suggest that roentgenotherapy is a better method of treatment of the axilla. The findings obtained in the advanced cases without distant metastases support this observation.

TABLE 3.—*Survival Rate for All Operable Cases in the Period 1941 to 1945 (Total Cases, 757)*

Years After Treatment	Number of Deaths from Cancer	Number Exposed to Risk	Chance of Dying in Any One Year	Survival Rate, Percentage
1.....	49	757	0.065	93.5
2.....	69	704.5	0.098	84.4
3.....	58	477	0.122	74.1
4.....	34	317	0.107	66.2
5.....	10	161.5	0.062	62.1

TABLE 4.—*Survival Rate for All Advanced Cases Without Distant Metastases in the Period 1941 to 1945 (Total Cases, 389)*

Years After Treatment	Number of Deaths from Cancer	Number Exposed to Risk	Chance of Dying in Any One Year	Survival Rate, Percentage
1.....	80	389	0.229	77.1
2.....	79	299.5	0.264	56.8
3.....	47	181.5	0.259	42.1
4.....	17	93	0.183	34.4
5.....	8	51.5	0.155	29.0

#### SURVIVAL RATE FOR ALL ADVANCED CASES WITHOUT DISTANT METASTASES IN THE PERIOD 1941 TO 1945

Treatment by simple mastectomy and roentgenotherapy was possible in only a limited number of cases, but, as in table 3, all patients whether fully treated or not, and all untreated patients are included.

The cases in this group are essentially those in which the disease was too advanced to be treated by radical mastectomy but was still to some extent localized, so far as could be ascertained by clinical and roentgenographic examination. The group therefore includes all cases in which the primary tumor was fixed to the pectoral muscle or to the underlying ribs and all cases in which there were fixed axillary glands or glands present in the supraclavicular region.

It will be seen from table 4 that 29 per cent of the patients were alive at the end of five years. This remarkably high figure clearly demonstrates that roentgenotherapy is an effective method of treatment of the axilla even when the axillary involvement is gross.

#### SURVIVAL RATE FOR ALL CASES IN THE PERIOD 1941 TO 1945

The analysis would not be complete without consideration of the results obtained in all the cases taken together.

It will be observed from table 5 that the five year survival rate for all cases referred during the period 1941 to 1945 was 43.7 per cent. It is interesting once again to compare this figure with that obtained during the period 1935 to 1940, when the main method of treatment

TABLE 5.—*Survival Rate for All Cases Referred in the Period 1941 to 1945 (Total Cases, 1,345)*

Years After Treatment	Number of Deaths from Cancer	Number Exposed to Risk	Chance of Dying in Any One Year	Survival Rate, Percentage
1.....	260	1,345	0.193	80.7
2.....	197	1,081	0.182	66.0
3.....	113	684.5	0.165	55.1
4.....	55	423	0.130	47.9
5.....	19	218	0.087	43.7

Calculation of the survival rate by the more usual methods gives almost the same result:

Total number of patients referred during 1941 and 1942 less patients who died from intercurrent disease.....	459
Number alive at the end of five years.....	197
Five year survival rate.....	42.9%

was radical mastectomy and postoperative roentgenotherapy. There were 790 cases referred during this earlier period, and the five year survival rate was 32.4 per cent.

#### THE EXTENT OF SELECTION OF CASES IN THE PERIOD 1941 TO 1945

All patients referred to the Royal Infirmary during this period have been presented. Reference to table 2 shows that 198, or 15 per cent, of the total number had clinical or roentgenographic evidence of distant metastases.

It will be recalled, too, that 11 deaths were added to the total to allow for any possible further postoperative deaths in patients operated on outside the Infirmary.

From 1941 to 1945 the annual number of patients referred was higher than at any other time. Part of this increase is explained by the fact that since 1941 an attempt has been made to ascertain the incidence of cancer of the breast in southeast Scotland, and, in order to do so, the general practitioners in the area were specially requested

to refer all cases to the Royal Infirmary, no matter how advanced they were. The evidence presented in figure 1 suggests that most cases are now being referred.

The significant feature in figure 1 is the fact that nearly all deaths now being recorded by the Registrar-General are occurring in patients already referred to the Royal Infirmary. All or nearly all patients must be referred for several years before such a high percentage is obtained. It may therefore be assumed that nearly all cases of cancer of the breast occurring in southeast Scotland are now being referred to the Royal Infirmary. From these observations it can be claimed with considerable

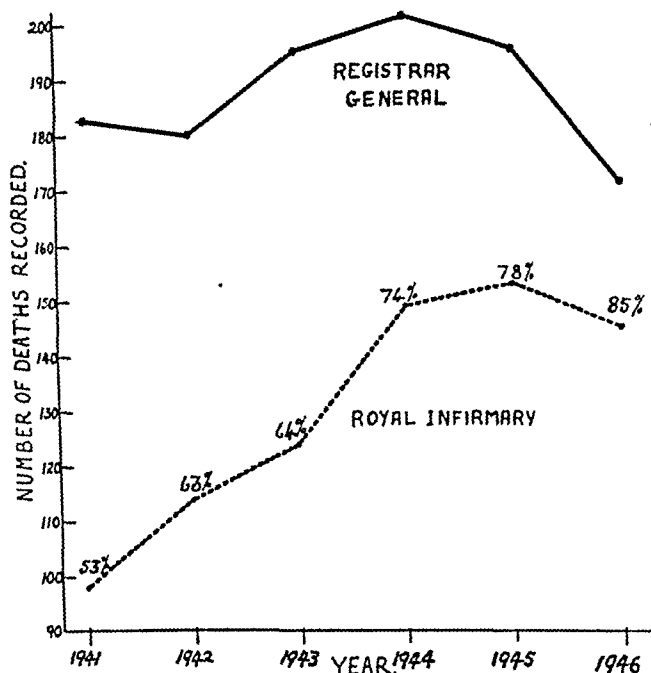


Fig. 1.—The number of deaths from cancer of the breast occurring in patients referred to the Royal Infirmary from the southeast of Scotland has been expressed as a percentage of the deaths recorded by the registrar-general from the same area.

confidence that the results obtained during the period 1941 to 1945 are based on unselected cases. In all probability the results are less influenced by selection than any figures hitherto published.

It is almost superfluous to add that if the reference of all advanced cases had not been specially requested, still higher survival rates could have been presented.

#### CARCINOMA OF THE BREAST WITHOUT DISTANT METASTASES

Table 6 is presented for interest. It shows the results obtained in all cases without clinical or roentgenologic evidence of distant metastases and is obtained by adding together cases in tables 3 and 4.

The table shows that when there was no evidence of distant metastases 1 of every 2 patients was alive at the end of five years.

#### TECHNIC OF SIMPLE MASTECTOMY AND ROENTGENOTHERAPY

A full account cannot be given of all the technical details of treatment by simple mastectomy and roentgenotherapy, but the following is a brief summary of the essential points.

The method of treatment is a combination of two procedures which must be coordinated if the best result is to be obtained.

The following points are of importance in the surgical aspect of treatment:

1. Preoperative preparation with iodine is contraindicated because it lowers the tolerance of the skin to roentgenotherapy.
2. The incision in the skin and the undermining of the skin flaps should be as limited as possible so that tissue spaces outside the area to be irradiated will not be contaminated with malignant cells liberated during the operation.

TABLE 6.—*Survival Rate of All Patients Without Clinical or Roentgenologic Evidence of Distant Metastases in the Period 1941 to 1945 (Total Cases, 1,146)*

Years After Treatment	Number of Deaths from Cancer	Number Exposed to Risk	Chance of Dying in Any One Year	Survival Rate, Percentage
1.....	138	1,146	0.120	88.0
2.....	148	1,004	0.147	75.0
3.....	105	658.5	0.160	63.0
4.....	51	410	0.124	55.2
5.....	18	213	0.085	50.5

3. Excessive skin should not be removed, for tension on the skin flaps may be associated with failure of the wound to heal and delay in the application of roentgenotherapy. Tightly stretched skin flaps do not tolerate irradiation well. Skin grafting does not overcome the difficulty, for grafts do not tolerate roentgen rays well.

4. When the primary tumor is mobile on the pectoral fascia, the fascia should not be removed, as this promotes fibrosis of the pectoral muscle. If the tumor is firmly fixed to the pectoralis major, the muscle should be removed together with the breast.

5. If there are no palpable axillary glands, dissection should not be performed, but superficial mobile glands in the subpectoral region and outside the axillary fascia may be removed. Any further dissection of the axilla will defeat the whole purpose of the method of treatment advocated.

6. If the patient is stout, it is better to carry out a radical mastectomy because in such patients it is difficult to deliver an adequate dose of roentgen rays to the axilla.

7. Supraclavicular glands should never be removed because these glands are easily and effectively dealt with by roentgenotherapy.

8. Adhesive should not be applied to the skin after the operation because this lowers the tolerance of the skin to irradiation.

The following points are of importance in postoperative treatment by roentgenotherapy:

1. Only one full course of roentgen ray treatment should be given. The practice of repeated courses at intervals of three to six months has no place in the treatment of any form of malignant disease when cure is to be attempted and is just as illogical as partial removal of a tumor at intervals of three to six months.

2. Roentgen ray treatment should be commenced as soon as possible after the operation; the usual interval is two weeks.

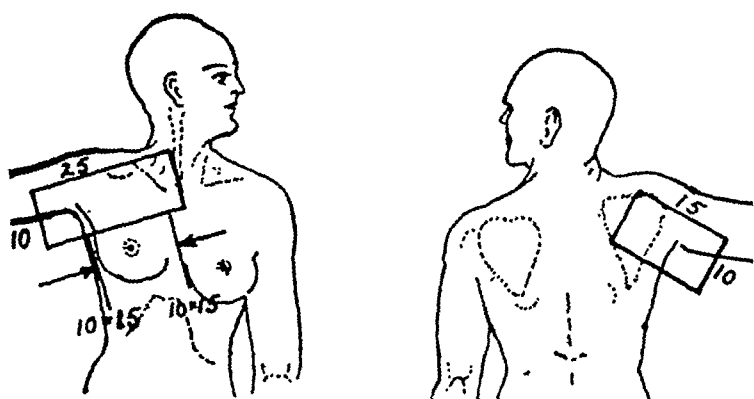


Fig. 2.—Arrangement of the fields in roentgenotherapy.

3. Four fields are used, and each field is treated every day. Irradiation of the axilla is carried out in two opposed fields, and the anterior field extends up to include the supraclavicular region. The thoracic wall must be treated by tangential or glancing fields so as to avoid pulmonary fibrosis. The arrangement of the fields is shown in figure 2.

4. An adequate dosage must be given, and in Edinburgh the patients receive a minimal tumor dose of 3,750 r in a period of three weeks. This is the same dosage as is given when clinically obvious local recurrences are treated, and it is important not to give less.

5. The x-ray apparatus must be sufficiently powerful to deliver an adequate depth dose in the axilla, and it is doubtful if effective roentgenotherapy can be given with an apparatus of lower voltage than 250 kilovolts. Heavy infiltration is employed, and the half-value layer of the beam is 3.7 mm. of copper.



## SUMMARY

An account has been presented of the method of treatment of cancer of the breast at present in use in Edinburgh. It must be accepted as representing but one direction in which the survival rates may be improved. There may be other better methods.

Considerable emphasis has been placed on the importance of assessing the true value of a method of treatment so that better methods may be recognized without undue delay. The view has been expressed that the publication of results of selected cases has greatly confused the issue and has tended to convey the impression that radical mastectomy is a highly successful method of treatment of cancer of the breast.

When radical mastectomy is the only method of treatment available and when all cases coming to a large general hospital are taken into account, the five year survival rate is unlikely to exceed 25 per cent.

A brief account of the method of treatment by simple mastectomy and roentgenotherapy has been presented. The five year survival rate for all cases coming to the Royal Infirmary in the period 1941 to 1945 is 43.7 per cent.

The most important feature of this method is the substitution of roentgenotherapy for surgical intervention in the treatment of the axilla. The decision to do so was taken because when the axilla is not involved by malignant cells it appears unnecessary to carry out an axillary dissection and when the axilla is involved the results of surgical dissection are poor.

The fact that a five year survival rate of 29 per cent was obtained in the advanced cases without distant metastases indicates that roentgenotherapy, even in such adverse circumstances, is an effective method of treating the axilla. It is therefore not surprising that this same method of treatment in operable cases should be associated with a survival rate much higher than that obtained by radical mastectomy.

A high standard of roentgenotherapy is essential, and adequate dosage must be given. It is most important to appreciate that simple mastectomy and a low standard of roentgenotherapy will be associated with results poorer than those obtained by radical mastectomy without any roentgenotherapy.

Figure 1 has been reproduced by kind permission of the editors of the *Proceedings of the Royal Society of Medicine*.

# ANESTHESIA IN TRAUMATIC CONDITIONS

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## GENERAL CONSIDERATIONS

THE PURPOSE of this paper is to present an outline of the procedures used to induce anesthesia in traumatic surgery. Underlying principles and general considerations will be emphasized at the expense of detailed discussion of various technics.

1. *Preparation of Patient.*—Correction of shock is an essential preliminary of anesthesia and operation in traumatic conditions. If immediate intervention is not a question of life or death, attention should be directed to certain problems before the induction of anesthesia.

If the patient is conscious, or other persons able to give pertinent information are present, a careful history should be taken. This should be followed by as thorough a physical examination as is permitted by the patient's injury, supplemented by the necessary and feasible laboratory examinations.

Such an examination often reveals conditions that need attention more urgently than the injury which was at first considered to be of primary importance. It has occurred that while an operating team was busy correcting a compound fracture of a limb the patient died of internal hemorrhage because of a ruptured spleen or kidney. The examination might also reveal preexistent pathologic conditions (such as heart disease or diabetes) which can be corrected to some extent and which might influence the surgeon regarding the type and the extent of the contemplated procedure.

Certain mechanical problems also need attention before the start of the anesthesia. If the injury followed a heavy meal, the stomach should be emptied whenever possible. It is also important to have the patient in a comfortable position that interferes the least with free respiration before the induction of anesthesia.

The treatment of shock includes the administration of analgesic and sedative drugs. If general anesthesia is to be employed, these drugs should be supplemented by parasympathetic depressants, atropine or scopolamine. These agents diminish the secretions of the upper respiratory and gastrointestinal tracts and diminish vagus irritability. Addi-

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tional doses of sedative and analgesic drugs should also be administered, if necessary. Great caution should be exercised in the administration of these drugs. It should be kept in mind that patients in shock, or just out of shock, with perhaps a suboptimal blood volume, are extremely sensitive to depressants and need considerably smaller doses than would correspond to their age and weight. Furthermore, the time interval between the administration and the action of depressants is often delayed in these patients, and often a second dose has been administered before the first dose had time to exert its full effect. This and the fact that the decomposition and elimination of drugs can also be delayed in injured patients might cause severe overdosage. Such overdosage can become even more serious if general anesthesia is superimposed on it. Morphine is especially dangerous in this respect, and extra care should be exercised in its administration to injured patients.<sup>1</sup> It should be administered only before anesthesia if the patient is actually in pain despite the fact that the previous analgesic dose had ample time to exert its effect or if the procedure is painful and the anesthetic agent to be used is not potent (nitrous oxide and oxygen) or has a relatively weak analgesic effect (thiopental sodium, U. S. P.). If only sedation is desired, one of the short-acting barbiturates (e.g., pentobarbital sodium) and/or scopolamine gives more sedation, with less accompanying respiratory depression, than morphine.

*2. Anesthetic Agents.*—The agents used to produce surgical anesthesia might be divided into two groups. The first group is composed of agents that impede conduction of the peripheral nerves. This group can be subdivided into the so-called local anesthetic agents and cold. Perhaps the most often used local anesthetic agents are procaine hydrochloride, piperocaine hydrochloride (metycaine hydrochloride®), tetracaine hydrochloride (pontocaine hydrochloride®) and dibucaine hydrochloride (nupercaine hydrochloride®). Their potency, toxicity and duration of action follow the order in which they are given here. The rapid intravascular injection of the local anesthetic agents might have serious consequences. The possibility of allergy to these agents also has to be kept in mind, especially in regard to patients with a history of allergy (hay fever, asthma and other conditions). A 1:1,000 solution of epinephrine and a 2.5 per cent solution of thiopental sodium (pentothal sodium®) should always be at hand when local anesthetic agents are used. The intravenous administration of 0.1 to 0.2 cc. of epinephrine can be of life-saving importance in the presence of allergic manifestations, and thiopental sodium is the antidote of choice against convulsions caused by the intravascular administration of local anesthetic agents.

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1. Beecher, H. K.: Delayed Morphine Poisoning in Battle Casualties, J. A. M. A. **124**:1193-1194 (April 22) 1944.

Cold has been used in the form of prolonged ice packs to produce conduction anesthesia.

The general anesthetic drugs are divided into inhalation, intravenous and rectal agents. The inhalation agents can be subdivided into gases and vapors. The most often used gases are nitrous oxide, ethylene and cyclopropane in this order of potency. Nitrous oxide or ethylene mixed with at least 20 per cent of oxygen produces moderate to good analgesia and amnesia, ethylene more so than nitrous oxide. Cyclopropane produces much deeper anesthesia than these two agents, with complete analgesia but sometimes inadequate relaxation. Ethylene and cyclopropane are explosive in anesthetic concentrations and have been the cause of many fatal explosions. Cyclopropane sometimes causes sudden serious cardiac disturbances.

Ether, vinyl ether (vinethene®) and chloroform are fluids with low boiling points, and their vapors are used to produce anesthesia. Their potency and toxicity increase in the order given. They are capable of producing deep anesthesia with relaxation, but the relaxation produced by vinyl ether is not always complete. Ether and vinyl ether are also explosive but less so than ethylene and cyclopropane.

Thiopental sodium is the almost exclusively used intravenous anesthetic agent. It produces good amnesia but only fair analgesia and poor relaxation. The reflex irritability of the vagus nerve seems to be increased under light anesthesia induced with this agent, and this explains the sometimes fatal laryngeal spasm that occurs when it is used.<sup>2</sup>

Tribromoethanol solution (avertin®) is the most often used rectal analgesic agent, but it has little place in anesthesia for the surgical treatment of traumatic conditions.

In the last few years curare and curare-like agents were introduced in the field of anesthesia. They produce more or less elective depression of the neuromuscular junctions, thereby causing good muscular relaxation. They produce no amnesia or analgesia and therefore are always used in combination with other anesthetic agents. Since they frequently cause complete transient respiratory paralysis, they should be used only if adequate personnel and equipment are available for the administration of oxygen endotracheally under positive pressure.

*3. Methods of Anesthesia.*—The types of anesthesia useful in traumatic surgery may be classified as conduction anesthesia, inhalation anesthesia, intravenous anesthesia, rectal anesthesia and combination or balanced anesthesia.

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2. Burstein, C. L.: Effect of Some Short Acting Barbiturates on the Patency of the Glottis, *Proc. Soc. Exper. Biol. & Med.* **37**:267-268 (Oct.) 1937.

Conduction anesthesia comprises local infiltration, regional block, nerve block, epidural and caudal anesthesia, spinal anesthesia and refrigeration anesthesia. The employment of local infiltration and regional block, often used in the reduction of closed fractures or the suturing of tissue lacerations, does not need much comment. Caudal anesthesia has not been used frequently in cases of trauma. The use of nerve block is gaining increasing popularity, in the surgical treatment of traumatic conditions. It has proved useful in cases of injury of the head, face, jaw and neck, in which close relationship with the upper airways often makes it desirable to work on a conscious patient. It is also useful in injuries involving the upper extremities. Brachial block anesthesia makes it possible to work in comfort on patients who still maintain to some extent the voluntary muscle movements of the involved area, which is helpful in cases of injuries of the tendons and nerves.

In traumatic surgery, spinal anesthesia should be used with great caution. It should be limited to cases involving the pelvic girdle and the lower extremities, and the level of spinal anesthesia should not exceed the tenth dorsal segment. Extensive crush injuries, and possible involvement of the spine, spinal cord or central nervous system, as well as shock and unreplaced loss of blood, are absolute contraindications to the use of spinal anesthesia. The choice of hypobaric and hyperbaric solutions makes it possible to administer the spinal anesthesia with the patient lying on either side, and this is sometimes important in cases of trauma.

Refrigeration anesthesia is carried out by packing the involved limb in chipped ice for several hours. It is mainly used when amputation is to be performed for extensive crush injury, gangrene or overwhelming infection. It not only permits painless performance of the operation, but it also minimizes the risk of generalized infection and prevents the absorption of toxins while the patient is being prepared for operation.

Inhalation anesthesia may be administered by the open, semiclosed and closed methods. The so-called open methods comprise the open drop, endopharyngeal and endotracheal insufflation technics. These methods do not require provision for the absorption of carbon dioxide, because the carbon dioxide produced leaves the body easily. The main advantage of these methods is that there is the least resistance in the way of respiration. Disadvantages of the method are that it is wasteful, produces lower oxygen concentration in the inhaled atmosphere and cannot be used with gaseous anesthetic agents. The open method is indicated for extremely young and extremely old persons and for debilitated patients. It is also used extensively for injuries of the head

and brain, in which the use of cautery is important, since the danger of explosion with the open method, especially if air is used as the vehicle for the anesthetic agents, is greatly reduced.

The semiclosed method is a transition between the open and the closed method. It combines some of the advantages and disadvantages of these two methods. It is used extensively in the administration of nitrous oxide-oxygen mixtures to insure a more or less constant nitrous oxide-oxygen concentration. It is also used in the form of the Flagg<sup>3</sup> can in combination with endotracheal tubes. The Flagg can offers little resistance to respiration, and the indications for its use coincide with those for endotracheal insufflation.

The closed method can be used with or without an endotracheal tube. It requires a close-fitting mask or, if an endotracheal tube is used, an inflatable cuff, or thorough packing of the pharynx with gauze can be substituted for the mask. The carbon dioxide produced has to be absorbed by soda lime or barylime absorbers. The advantages of the method are its economy, the ease with which a constant plane of anesthesia can be maintained, its applicability to gaseous anesthetic agents, the high oxygen atmosphere and the possibility of positive pressure anesthesia. Its disadvantages are greater stress on respiration and circulation, greater explosive hazard and greater danger of overdosage in unskilled hands. The closed method might be used with or without an endotracheal tube. The endotracheal tube can be inserted through the mouth or nose. When the injury interferes with a free airway and general anesthesia has to be used, the endotracheal tube is inserted after cocainization of the pharynx and larynx, before the start of anesthesia. It is remarkable how well patients with respiratory obstruction and hypoxia will tolerate the insertion of an endotracheal tube while conscious. The endotracheal tube can be inserted either "blindly" or with the help of a laryngoscope.

In some cases the nature of the injury makes it imperative to insert a tracheotomy tube under local anesthesia before general anesthesia can be started. Even when this heroic measure does not seem to be indicated at the start of anesthesia, a tracheotomy set and a surgeon able to perform a rapid emergency tracheotomy should always be at hand when anesthesia is administered to patients with injuries of the head, face or neck. Injured patients tolerate hypoxia or anoxia badly, and if the insertion of an endotracheal tube is technically impossible at the onset of hypoxia, there should be no hesitation in inserting a tracheotomy tube.

Positive pressure anesthesia is indicated whenever the injury involves the pleural space or when the corrective procedure involves the intentional or accidental opening of the pleural space. Care should

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3. Flagg, P. J.: *The Art of Anesthesia*, ed. 6, Philadelphia, J. B. Lippincott Co., 1939.

be taken that the positive pressure should not be excessive and that it should be administered intermittently. The circulation of the seriously injured patient does not tolerate continuous positive pressure anesthesia over a prolonged period. The important thing is to inflate the lung of the open side intermittently and keep it inflated while airtight closure of the pleura is being carried out.

Some methods of inducing anesthesia which involve transitory respiratory paralysis (curare) might also require positive pressure anesthesia.

Intravenous anesthesia is usually induced by thiopental sodium, and more recently procaine hydrochloride is also being used intravenously to produce analgesia suitable for the completion of minor procedures. Thiopental sodium alone is useful in the surgical treatment of traumatic conditions, but it is even more so in combination with other agents. Induction with this agent is pleasant and swift, and if it is administered properly and over not too long a period, recovery is rapid. It has to be kept in mind, however, that in safe concentrations its analgesic potency is not too high. Pain reflexes originating in the skin are obtunded poorly. For painful procedures, it is advisable to combine it with local or nitrous oxide-oxygen anesthesia. This is especially true with adolescents and vigorous young adults. If painful procedures are attempted with its use alone, often so much has to be used that the patient sleeps many hours postoperatively. The incidence of laryngeal spasm is also much increased if painful procedures are attempted under thiopental sodium anesthesia. Another frequent cause of laryngeal spasm with this anesthesia is manipulation in the region of the head, face and neck. Such procedures should be done under thiopental sodium anesthesia only after the local anesthetization of the pharynx and larynx and the insertion of an endotracheal tube. Equipment and personnel should always be at hand for endotracheal intubation whenever this agent is administered, and a generous dose of atropine or scopolamine should precede its use. The subcutaneous injection of morphine forty-five to sixty minutes preoperatively will also markedly decrease the amount of thiopental sodium necessary.

In recent years, various neuromuscular depressants have gained widespread use in anesthesia. Curare (*intocostrin*®) and *d*-tubocurarine chloride are the best known of these agents, and dihydro- $\beta$ -erythroidine has also been used to some extent. They are always used in combination with other anesthetic agents, and it is well to remember that the dose of these agents is much less when used in combination with ether and thiopentothal sodium than if they are used with cyclopropane. Since the margin between the dose producing muscular relaxation and that producing respiratory depression is often small, it is wise to administer

the expected amount in fractional doses and to stop when the necessary relaxation is obtained. The use of neuromuscular depressants without an endotracheal tube is dangerous.

The use of combined or balanced anesthesia is often indicated when the patient is severely injured. The indications of the different combinations will be discussed with the choice of anesthesia for the various procedures.

*4. Choice of Agents and Methods.*—The safety of the patient, the working conditions of the surgeon and the comfort of the patient, in the given order, are the chief considerations in the choice of the anesthetic agent and method. In choosing the most suitable anesthesia, attention has to be paid to age, physical condition, possible underlying pathologic processes, site of the injury, extent of the surgical procedure, available drugs and equipment and the familiarity of the anesthetist with the different methods. Extremely young and extremely old patients are more sensitive to hypoxia and to depressants of the central nervous system. Certain diseases make the patient especially sensitive toward certain agents; e. g., patients with hypothyroidism or hepatic insufficiency are extremely sensitive to morphine and noncompensated diabetic patients with acidosis are most sensitive to thiopental sodium. It is also a better practice to allow the anesthetist to use a method that would perhaps be a second choice than to make him use agents or methods that might seem to be indicated but with which he is less familiar.

*5. Conduct of Anesthesia.*—Certain points have to be kept in mind regarding the conduct of anesthesia in the injured patient. Induction should be as smooth as possible because excitement, straining, retching or vomiting might start fresh hemorrhage or increase the deformity and trauma present. Thiopental sodium or nitrous oxide and oxygen should be used for induction, and more emphasis should be placed on smoothness than on speed. It is often advisable to give a little thiopental sodium before the administration of the local anesthetic agent. Better local anesthesia can be produced in the quiet patient, and in the end considerably less of this drug and less local anesthetic agent will be used than if the process had been reversed.

The injured patient should be carried in the lightest possible plane of anesthesia. This can be done satisfactorily by the judicious combination of the various agents and methods.

It cannot be emphasized too often that the injured patient needs adequate oxygenation. The agents used have to be so chosen that at least 20 per cent oxygen, but preferably more, should be in the inhaled atmosphere. The use of nitrous oxide in concentrations greater than 80 per cent is not permissible. If there is any respiratory obstruction,



this should be corrected immediately by changing the position of the patient and inserting a pharyngeal airway or, if these methods do not relieve the obstruction, by the use of an endotracheal tube or, in extreme cases, tracheotomy.

Adequate relaxation should be provided during the operation. A struggling surgeon cannot do the best job, and in the end more harm will come to the patient than if better relaxation had been produced by deeper anesthesia or by the use of neuromuscular depressants.

The anesthesia should be so planned that the patient should recover consciousness shortly after the end of the operation.

Special attention should be given to the circulation during anesthesia. Eventual loss of blood should be replaced at once. Injured patients often go into shock again in the course of operation. This should be recognized and combated by the administration of a judicious combination of blood, plasma and dextrose solutions. If the patient is in shock, the administration of the anesthetic agent has to be decreased or discontinued.

6. *Possible Complicating Factors.*—One of the most frequent complicating factors is hypoxia. This can be due to mechanical interference with the airway (obstruction or laryngeal spasm), respiratory depression from injury, the anesthetic agent or method, loss of blood, circulatory failure, lack of oxygen in the inhaled mixture, pneumothorax or reduction of the respiratory surface.

Aspiration of stomach contents, blood, pus or foreign bodies is also encountered in injured patients. This complication might require bronchoscopy before the surgeon can proceed with the corrective procedure.

Operative shock and hypersensitivity to anesthetic agents have been mentioned, and, last but not least, chronic alcoholism must also be remembered. Persons with chronic alcoholism sustain injuries more often than any other group, and bitter experience has shown us that induction of anesthesia in these patients can be exceedingly troublesome, even in the hands of experienced anesthetists.

7. *Postoperative Care.*—To a certain extent, the immediate postoperative care is also the responsibility of the anesthetist. Patients in shock, or with low blood pressure, should be kept on the operating table in a moderate Trendelenburg position. They should be well covered, and oxygen should be administered. They should be moved only after suitable intravenous therapy has restored their blood pressure to a normal level. To avoid unnecessary moving, their beds should be wheeled into the operating room.

Care should be taken that the patient is left in bed in a position that provides for a free airway. The nursing personnel must be

instructed that the patient should be watched carefully so that a change of position or the removal of the oral or nasal airway will not cause respiratory obstruction. Sometimes bandages applied when an endotracheal tube or pharyngeal airway is still in place may interfere with respiration when these are removed. Postoperative edema of the larynx, bleeding or edema in or around the soft parts of the upper airway may also cause severe hypoxia. If the injury involves the head, face or neck, a tracheotomy set should always be kept at the bedside until the patient is fully conscious and the danger of respiratory obstruction is excluded. Massive atelectasis must be considered and, if present, corrected by suction bronchoscopy.

The anesthetist should prescribe individually the necessary analgesic and sedative agents. The judicious combination of analgesics (morphine) and sedatives (barbiturates) will minimize respiratory depression and provide comfort for the patients with relatively small quantities of drugs. The use of such combinations, instead of the routine use of large doses of morphine alone, should be encouraged.

#### SPECIAL PART

*1. Anesthesia for Injuries of the Head, Face, Jaw and Neck.*—Provided that there is no respiratory embarrassment and that no respiratory obstruction can be expected, the anesthesia of choice for these injuries is some form of conduction anesthesia. If local anesthesia, field block or nerve block is to be supplemented by some form of light inhalation or intravenous anesthesia, the latter should be started before the local anesthesia, when the patient is easily accessible to the anesthetist. The patient should be carried into the plane in which the anesthesia is to be maintained and put into the operative position, and the respiration should be checked again. If any respiratory difficulty has developed it must be corrected, if possible, by the use of a pharyngeal airway or by endotracheal tube if necessary. Oxygen should be administered freely either by nasal catheter or by endotracheal insufflation; if the supplementary anesthesia is inhalation anesthesia at least 30 per cent oxygen should be added to the inhaled mixture. The surgeon should rely on the local or block anesthesia and should consider the thiopental sodium or nitrous oxide-oxygen anesthesia as an auxiliary measure.

If there is any respiratory difficulty preoperatively, or respiratory difficulty can be expected in the course of operation, the anesthesia of choice is endotracheal anesthesia. The agent can be endotracheally administered ether or thiopental sodium with endotracheally administered nitrous oxide and oxygen, depending on the type of injury. If the patient's respiratory condition is such that adequate oxygenation can be maintained during induction with ether anesthesia and the

surgeon does not want to use cautery, ether should be used endotracheally. If the condition warrants rapid induction, the endotracheal tube can be inserted under thiopental sodium and curare anesthesia. In this case, however, the pharynx and the larynx should be sprayed under vision with a local anesthetic agent before the introduction of the endotracheal tube. Spraying of the cords with a local anesthetic agent might decrease the danger of bronchial spasm that is sometimes seen with the use of curare.

Whenever an endotracheal tube and thiopental sodium are used together, oxygen alone or nitrous oxide and oxygen should also be administered by the semiclosed method. The endotracheal tube might be introduced through the nose or through the mouth, whichever is more suitable for the contemplated procedure. If an endotracheal tube without a cuff is used, the pharynx should be packed around the tube to prevent aspiration.

*2. Injuries of the Chest, Back, Spine and Spinal Cord.*—For penetrating injuries of the chest endotracheally administered ether is the anesthetic of choice. Positive pressure anesthesia necessary for the reexpansion of the collapsed lung can be given with an endotracheal tube and a closed system. Some clinics prefer to use cyclopropane instead of ether in their open chest operations, but I feel that although cyclopropane is indicated at times in the average case the use of ether is more advantageous.

Unless there is acute hypoxia, the collapsed lung should be expanded only when the surgeon has access to the pleural cavity. Reexpansion of the lung may start fresh bleeding that might be fatal unless it can be dealt with immediately. The lung should be kept inflated until it regains its normal appearance. After that it should be kept expanded or allowed to collapse as the surgical procedure may require. It should be kept in mind that if the surgeon has to work with a collapsed lung, the operation should be interrupted and the lung expanded for a minute or so every twenty minutes. It should also be remembered that excessive positive pressure is not well tolerated by debilitated patients. No effort should be made to keep the lung fully expanded over a prolonged period. The important thing is to expand the lung fully under vision before the wound in the chest is closed and keep up the necessary positive pressure while airtight closure of the wound is being carried out.

Nonpenetrating injuries of the chest and injuries to the back, spine and spinal cord should be treated according to the principles discussed previously. Whenever possible, some kind of conduction anesthesia should be used, supplemented as necessary with oxygen, nitrous oxide and oxygen or thiopental sodium.

If the operation is to be done in the prone position, it is advisable to use an endotracheal tube. Injured patients tolerate the prone position poorly, and whenever possible the operation should be carried out with the patient on his side or in the semiprone position if the operative field is in the dorsal part of the body.

Another instance in which an endotracheal tube is a necessity is when injury to the cervical region of the spine and the cord is present. The endotracheal tube should be inserted with great caution, without changing the position of the head in any direction. Whenever possible, the surgeon should be present at the intubation and should be consulted as to the change in position advisable. If the intubation cannot be carried out easily, it is far better judgment to use a tracheotomy tube than to risk the patient's life by further attempts.

Spinal anesthesia should be avoided in all cases in which the spine, spinal cord or brain is, or might be, injured. If the spinal tap reveals any abnormality in a case in which it was not suspected, the anesthesia should be changed.

*3. Injuries of the Upper Limbs and the Shoulder Girdle.*—The anesthesia of choice for operations on the arm and hand is brachial plexus block. Wrist block or elbow block can also be used if the injury is below the corresponding level. For extensive operations on the shoulder girdle the use of general anesthesia, often with an endotracheal tube, is necessary.

Closed reduction of fractures and dislocations can be satisfactorily carried out under light thiopental sodium anesthesia. A good practical rule is never to give an additional dose of thiopental sodium in the fluoroscopy room while the lights are out. Local infiltration with procaine hydrochloride often is also of use for closed reduction of fractures.

*4. Injuries of the Pelvis and the Lower Limbs.*—The anesthesia of choice for operations on the pelvis and the lower extremities after simple injuries is spinal anesthesia. The level of anesthesia can and should be kept low enough to avoid unwarranted side effects due to paralysis of the vasoconstrictors of the splanchnic area. With severe crush injuries of the pelvis and lower limbs involving more than one bone, especially if the patient is in shock due to loss of blood, cyclopropane is the best anesthetic agent.

Because of the frequency of this condition, the anesthetic management of patients with a fractured hip should be considered in a little more detail. Since this condition occurs mostly in the aged, the effects of trauma are superimposed on debility caused by age and preexistent disease. Because of the danger of pneumonia, there is a tendency to rush the patients into the operating room as soon after the accident as possible. Since the advent of sulfonamide drugs, penicillin and streptomycin, the

danger of pneumonia in these patients has been greatly decreased, and experience has shown that it is a better policy to allow them to recover from the physical and psychologic effects of trauma before undertaking the operative procedure. Often these patients, if not suffering from cardiac failure, have a markedly decreased cardiac reserve which needs attention before operation.

The anesthesia of choice for fractures of the hip is either low spinal anesthesia or the combination of thiopental sodium, nitrous oxide-oxygen and local anesthesia. Premedication should be given sparingly; one half to one third of the regular dose usually will be sufficient. The dose of the spinal anesthetic agent should also be small. Results with the combination of nitrous oxide and oxygen, thiopental sodium and a local anesthetic are gratifying. This combination should be used in the presence of myocardial or coronary disease.

Anesthesia should be induced with a small dose of thiopental sodium and then nitrous oxide and oxygen in a 60 to 40 or a 50 to 50 per cent concentration should be administered by the semiclosed method. The reduction of the fracture can be carried out with ease under this anesthesia. The site of the incision should then be infiltrated with 0.5 to 1 per cent procaine hydrochloride. Usually the amount of thiopental sodium necessary for the whole procedure is well below 0.5 Gm., and the patients awake shortly after administration of nitrous oxide and oxygen is discontinued.

Both the surgeon and the anesthetist must realize that hip nailing, and this is also true for operative procedures on any of the large bones of the skeleton, is apt to result in a severe fall of blood pressure and sometimes in surgical shock. Blood for transfusion should be readily available and should be used prophylactically during the procedure.

In cases of extensive crush injuries, gangrene and anaerobic infections of the lower extremities requiring amputation, refrigeration anesthesia proves to be useful. One of its main advantages is that it decreases the absorption of toxins and thereby improves the general condition of the patient while he is being prepared for operation.

The use of ankle block anesthesia for injuries of the foot also deserves a place in the anesthetists' armamentarium.

5. *Burns, Anaerobic Infections, Thrombophlebitis, Phlebothrombosis and Injuries of the Vessels.*—The treatment of extensive burns always has been a difficult problem. Despite the enormous progress made in this respect in the last years, the margin of safety is low in handling patients. Experience has shown that for the débridement of extensive burns light thiopental sodium anesthesia is better tolerated than ether. However, this is true only if the thiopental sodium is administered with extra care by a person who fully understands the pathologic changes produced by burns.

Recently procaine hydrochloride has also been used intravenously for the dressing and débridement of burns. I have no personal experience with this method, but those who use it report that these procedures can be carried out with little discomfort on conscious patients under intravenously administered procaine hydrochloride.

In contrast, thiopental sodium anesthesia should not be used in patients with anaerobic infections.

The use of paravertebral sympathetic block has proved to be a valuable adjunct in the treatment of traumatic conditions. Trauma is often accompanied with thrombophlebitis or with phlebothrombosis of the lower extremities. Although sympathetic block will not replace ligation of the superficial femoral veins in thrombophlebitis, its value in the treatment of phlebothrombosis of the deep veins is unquestionable. The prolonged arterial spasm that often accompanies injuries is also benefited by this procedure.

#### SUMMARY

In summary, it should be emphasized that preanesthetic examination, preanesthetic medication, choice of anesthesia, conduct of anesthesia and postoperative care are equally important corollaries of the surgical treatment of the injured patient. Good oxygenation and the prevention of aspiration of blood and foreign material are perhaps the two most important considerations in the conduct of anesthesia. If the anesthetist remembers that the order of importance is the safety of the patient, making the work of the surgeon as easy as possible and, lastly, the comfort of the patient, then he has done his duty to the seriously injured.

## SHORT RADIUS

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**N**ORMAL appearance and function of the forearm depends on the existence of freely movable superior and inferior radioulnar articulations, adequate motor power in the musculature of the forearm and the preservation of the normal length relationships between the radius and the ulna. Since pronation and supination of the forearm takes place around an axis which extends from the head of the radius to the head of the ulna, any disproportion in the length of either bone necessarily leads to some disturbance in function of the upper or the lower radioulnar joint.

At the lower joint, the situation is further complicated by the fact that the carpus articulates with the lower end of the radius and not with the ulna. Since the carpus follows the radius, anatomic derangement of the distal radioulnar joint leads to deformity which is characterized by a prominence of the ulnar head on the dorsum of the hand. This has been improperly designated as a "dislocation of the ulna" or a "Madelung-like" deformity of the wrist.

The latter designation is especially to be deprecated since it completely ignores the fundamental difference in the pathologic changes between the two conditions. In discussing Madelung's deformity, Ghormley<sup>1</sup> properly noted that "many cases have been reported which are not true Madelung's deformity, although they present an appearance similar to the condition. These may be cases of old malunited fractures, residual deformity from epiphysitis, or osteomyelitis, dyschondroplasia with radial deformity, congenital malformation of the radius, chronic arthritis and so forth."

Anton, Reitz and Spiegel<sup>2</sup> define Madelung's deformity as an "idiopathic, progressive curvature of the radius due to a dyschondroplasia of the inferior radial epiphysis resulting in a deformity of the wrist giving the appearance of an anterior (or more rarely a posterior) subluxation of the ulnar head." In the more advanced cases there may be secondary adaptational changes in the ulna. Primarily, however,

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1. Ghormley, R. K., and Pollack, G. A.: Osteochondrodystrophy of the Inferior Radio-Ulnar Epiphysis (Madelung's Deformity), Proc. Staff Meet., Mayo Clin. 4:759 (Nov.) 1929.

2. Anton; Reitz, and Spiegel, cited by Ghormley.<sup>1</sup>

the pathognomonic feature of Madelung's disease is the progressive curvature of the radius. This has led to its designation as radius curvus. In its mildest manifestations there is no disparity in length between the two bones, so that the curved radius (radius curvus) may be readily differentiated from the short radius (radius parvus) here under discussion. This can be seen in the following instance.



Fig. 1 (case 1)—The left hand is identical in appearance with the right. The ulnar head is at its normal level with respect to the radius. The lower end of the radius is curved forward. The radiocarpal mass is displaced forward, and the position of the ulnar head is similar to that seen in "so-called posterior dislocation of the ulna."

Case 1.—Natividad O., a Puerto Rican aged 24, presented herself for the treatment of bilaterally prominent ulnar heads. There was slight, if any, limitation of function, and the power of grasp was excellent. The roentgenograms of the two hands were practically identical and disclosed an abnormality which had been called "a posterior dislocation of the ulna" (fig. 1). Though the ulnar head



appeared to be displaced dorsally with respect to the radius, it can be observed that it is about at its normal level. On the other hand, the lower end of the radius is curved excessively forward so that the inferior radioulnar joint is disrupted. The carpal mass follows the radius, and therefore "anterior dislocation of the carpus" would much more closely describe the anatomic situation.

It was apparent that the forward displacement of the radiocarpal mass with respect to the ulna could be corrected only by means of a cuneiform shortening of the radius. Since the patient's complaints were entirely of an esthetic nature and there was no impairment in function, operation was not advised.

Madelung's deformity may be simulated by other conditions, and its specific pathogenesis is not fully understood. Bunnell<sup>3</sup> observed that "the deformity is from an epiphyseal growth defect in the lower end of the radius that does not make its presence known until the ages of 10 and 15 with 12 as the average. It is bilateral in two thirds of the cases and four times as frequent in girls. In at least 10 per cent it is hereditary." All these characteristics would seem to indicate something more than simple interference with growth at the inferior radial epiphysis. Even though it may be characterized by a prominence of the ulnar head on the dorsum of the hand, Madelung's deformity must be sharply differentiated from the "so-called dorsal dislocation of the ulnar head" seen in cases of short radius.

Shortening of the radius, or radius parvus, may arise from a number of different causes. The types may be conveniently divided into two groups: those which occur before skeletal maturity has been reached and those which occur after. In the former group it is primarily to those which interfere with epiphyseal growth that attention must be directed. In these it is to be noted that premature closure of the epiphysis may lead to a shortening of the radius and even to an alteration in the direction of the inferior articular surface but seldom if ever to a true curvature of the lower end of the bone. This is seen in the following case.

CASE 2 (previously reported<sup>4</sup>).—Toby S., aged 9, was first seen in December 1936, about three months after her wrist had been twisted by a school mate. The earliest roentgenograms taken at another hospital could not be examined, but a report indicated that the child had suffered a volar displacement of the distal end of the radial epiphysis. At the time of her admission there was no evidence of any acute inflammatory signs. The left wrist appeared larger than the right and manifested a sharp volar and radial displacement. The ulnar head was prominent on the dorsal surface, but there was no evidence of weakness of the wrist at this time. The roentgenogram showed a wide metaphysis and an irregular cup-shaped lower radial epiphysis. The volar half of the epiphysis seemed to have undergone premature closure. The dorsal half was narrowed

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3. Bunnell, S.: *Surgery of the Hand*, Philadelphia, J. B. Lippincott Company, 1944, p. 625.

4. Milch, H.: So-Called Dislocation of the Lower End of the Ulna, *Ann. Surg.* **116**:282 (Aug.) 1942.

but still open, and its growth undoubtedly accounted for the excessive forward inclination of the articular surface. The ulna, unaffected by the earlier trauma, had continued to grow normally and projected downward below the level of the styloid process of the radius.

It was at first believed that the "ulnar dislocation" could be overcome by manipulation. After failure of this ill advised effort, osteotomy was decided on. This too was completely unsuccessful in correcting either the angulation or the disparity in length (fig. 2 *A*). With the continued growth of the child, the dis-



Fig. 2 (case 2.)—*A*, anteroposterior view after osteotomy. The volar angulation can still be recognized. The disproportion in length has not been corrected. *B*, after subperiosteal resection the distal portion of the ulna has regenerated, but because of the presence of the carpus on the same plane, its lower portion has been deflected medially.

proportion in length became progressively greater, and she began to complain of increasing weakness of the wrist, limitation of rotation and a bony prominence on the dorsum of the wrist.

In October 1938 the child was readmitted for treatment of the "so-called posterior dislocation of the ulnar head." Lengthening of the radius did not hold out much hope of success, and it was finally decided to resect the lower end of the ulna according to the method described by Darrach. Immediately after the operation the patient appeared pleased with the disappearance of the lump and the radial deviation of her hand.

Within a short time, however, increasing width of the wrist was again noted, and the roentgenogram offered the explanation (fig. 2*B*). After the subperiosteal resection of the ulna, the hand was able to resume its normal position. However, as the lower end of the ulna regenerated, the outward pressure of the carpus against the plastic, newly grown tissue caused it to deviate medially, increasing the width of the wrist. In this position it did not impair rotation of the radius since the prominence previously noted on the dorsum of the wrist had been shifted medially and thus could not impinge against the proximal row of carpal bones.

Deformity of an identical nature may arise from ill advised fusions of the radiocarpal joint. Because of the likelihood of danger to the epiphyseal bone, plate fusions of the wrist should be undertaken with the greatest circumspection and if possible should be deferred until epiphyseal growth can no longer be jeopardized. If, however, surgical closure of the radial epiphysis is absolutely indicated, the epiphysis of the ulna should be simultaneously obliterated. Failure to accomplish this must lead to a disproportion in length of the bones of the forearm and the necessity of further operation. This is illustrated in the following instance.

CASE 3.—Joseph De L. was brought to the hospital in 1926 at the age of 2. A full term baby, he had been delivered instrumentally and had suffered birth palsy which affected the whole right arm. The earliest treatment consisted of immobilization on an abduction splint and had resulted in a considerable increase in the power of the shoulder girdle musculature. However, despite exercises and electrotherapy, paralysis of the wrist and a flexion contracture of the elbow persisted. To overcome the wristdrop and the contracture at the elbow, the arm was manipulated under anesthesia and a plaster of paris splint was applied. Further treatment was deferred because of the child's age.

In 1933 the patient, aged 9, was again admitted to the hospital for definitive cure of the wristdrop. This was accomplished by excision of the articular surfaces and the sliding of a bone graft from the lower end of the radius across the joint line to the proximal row of carpal bones (fig. 3*A*).

The result of this operation was far from happy. Arthrodesis was not complete, and though the wristdrop was overcome, the price of this triumph proved unduly great. While the graft had not caused ablation of the radiocarpal joint, it had led to premature closure of the dorsal half of the distal epiphysis. As a consequence, the volar portion continued to grow, causing the inferior articular surface of the radius to point dorsally. This growth was far below its normal rate, so that the ulna soon outstripped the radius in length. The ulnar head became prominent on the dorsum of the wrist and the hand deviated toward the radial side.

The roentgenogram (fig. 3*B*) was reported as showing "internal and posterior luxation of the ulna." The ulna is slightly longer than the radius. The epiphyseal lines of the radius and the ulna are uneven, that of the radius showing an upward inclination, with partial obliteration of its dorsal portion.

Despite these abnormalities there was relatively little restriction of rotation of the forearm at the inferior radioulnar articulation. This was believed to be due to the fact that after operation a disruption of the inferior radioulnar joint occurred. In consequence of this the

ulna projected downward along the medial aspect of the carpus instead of directly on it. When this occurs the disability due to so-called posterior dislocation of the ulna does not become manifest and equalization of bone length or resection of the ulna is not indicated except for esthetic reasons. The following instance illustrates this.

CASE 4 (previously reported<sup>5</sup>).—Rufus F., aged 38, was seen in 1945 presenting the typical appearance of a bilateral "dislocation" of the ulnar heads. Contrary to what is usually seen in cases of this condition, there was relatively

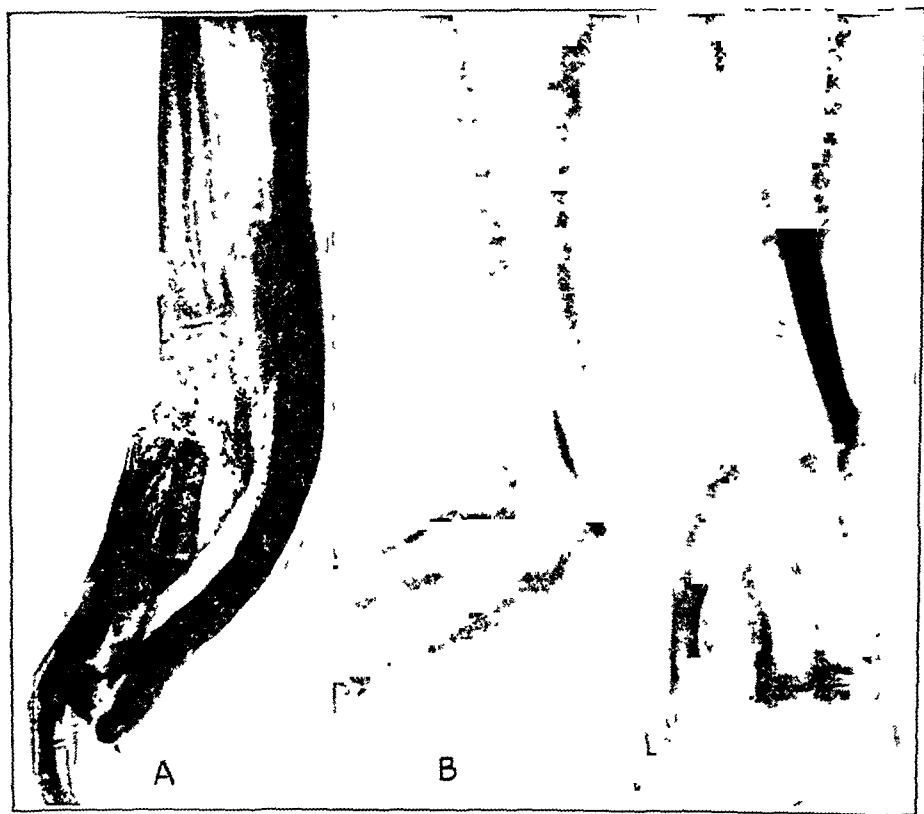


Fig. 3 (case 3).—*A*, roentgenogram in April 1933. Anteroposterior view shows relatively normal length relationship between radius and ulna. On the lateral view the bone graft can be seen extending from the metaphysis across the epiphyseal plate to the proximal row of the carpus. *B*, roentgenogram in November 1936. In the anteroposterior view the ulna is displaced medially and is so much longer than the radius that the styloid process of the ulna is at the level of the distal row of carpal bones. The inferior radioulnar joint has been disrupted, but there is no curvature of the radius. In the lateral view synchondrosis of the dorsal portion of the epiphyseal plate with dorsal angulation of the articular surface is to be noted.

little impairment of the range of rotation or the power of grasp in either hand. The roentgenogram (fig. 4) disclosed a definite shortening of the radius. The lower end of each radius was broad and gave the impression of premature fusion.

5. Milch, H.: Bilateral Ulna-Cuneiform Articulation, *Am. J. Roentgenol.* 61:80 (Jan.) 1949.

The sigmoid notch was irregular and clearly had not been articulated with the radial head for many years. The inferior radioulnar joint was completely disrupted and the ulnar heads articulated with what appeared to be facets on the medial aspect of both cuneiform bones. The right radial styloid process was not united and indicated a traumatic origin.

When closely questioned, the patient recalled that as a boy of 10 he had fallen headlong out of a tree and landed on both hands as if he were diving. Apparently no serious damage was noted at the time, because the entire treatment consisted of the application of volar splints. However, serious damage had been done the growing zone of both radial epiphyses, which had apparently been contused or compressed. With the passage of years these epiphyses showed retardation of



Fig. 4 (case 4).—Each radius is shorter than its associated ulna. The lower end of the radius is broad and gives the impression of premature ossification. The radioulnar joint is disrupted, and the ulnar head articulates with the carpal cuneiform on both sides

growth with gradual prominence of the ulnar heads and radial deviation of the hands. Because of lack of any ligamentous injury, the ulna had continued growing downward in its normal plane and had simply displaced the carpus radially. (This is similar to what happened in case 2 after resection of the ulna.) As a result of its constant pressure against the cuneiform bones, new articulations between the ulna and the radiocarpal mass had developed. The action of the inferior radioulnar joint was nullified, and rotary motion which normally occurs at this joint was now carried on across the ulnocuneiform joint without interference. Because of the absence of any impairment of function and the patient's disregard of the deformity, operative intervention was not deemed justifiable.

In addition to these purely traumatic types, premature epiphyseal closure may be the result of tumor formation, dyschondroplasia or infection. While the disproportion in length to which these epiphyseal conditions lead is striking and frequently progressive in nature, far more common causes for shortening of the radius are to be found in instances in which actual physical shortening occurs.

Among these is resection for fracture of the head of the radius. Watson-Jones<sup>6</sup> noted:

. . . if the upper end of the radius is too freely excised, it is so much shortened that the relatively long ulna gradually subluxates at the inferior radioulnar joint and pushes the hand over to the radial side. The patient complains of weakness of grip and aching pain in the wrist. In the adult this complication seldom occurs if the excision is confined to the head of the bones, and the neck and orbicular ligament are left undamaged. In children, on the other hand, excision of the head of the radius removes the epiphyseal line. The disproportion in length of the radius and ulna becomes steadily greater as the child grows and a more serious disability develops in the wrist.

Blount<sup>7</sup> has expressed the opinion that "there is no need during childhood for removing the radial head. . . . When the radial head is removed in a young child the inevitable sequel is a deformity of the wrist with radial deviation of the hand, shortening of the radius, weakness and sometimes pain."

Similar shortening may arise from either loss of continuity or angulation as a consequence of fracture of the shaft of the radius.

CASE 5.—Sylvia M., aged 22, was seen in 1942. When she was 5 years old, she was involved in some sort of accident which resulted in a fracture of the radius. For the treatment of this, an open operation was performed. Infection developed, and prolonged treatment, with ultimate loss of a portion of the radial shaft, was necessitated. As a consequence of this the hand and forearm were markedly underdeveloped. The ulna, which was shorter than the opposite normal ulna, projected on the dorsum of the hand. The hand was deviated toward the radial side and seemed to jut out from the side of the forearm. There was pronounced limitation of rotation in the forearm, but the power in the fingers was good, so that with the hand in pronation the patient was able to work as a typist. The roentgenogram (fig. 5A) disclosed the deformity of the radius, with pseudoarthrosis in the midshaft. The ulnar head projected downward to below the levels of the carpometacarpal joints.

Because of the patient's youth at the time of injury, the ultimate disproportion in length was much greater than that which would have taken place in an adult in similar circumstances. While the esthetic

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6. Watson-Jones, R.: *Fracture and Joint Injuries*, ed. 3, Baltimore, Williams & Wilkins Company, 1946, p. 474

7. Blount, W. B.; Schaffer, A. A., and Johnson, J. H.: *Fracture of Forearm in Children*, J. A. M. A. **120**:111 (Sept. 12) 1942.

consequences are proportionately less disturbing, the functional result is qualitatively analogous in nature and the degree of impairment is largely of a quantitative nature.

CASE 6.—Samuel G., aged 45, was seen in October 1945 after an injury to the left forearm some three months before. A neighborhood physician applied a plaster without making any attempt at reduction. Subsequent examination disclosed that the radial styloid process was elevated in relation to the ulnar styloid process.



Fig. 5.—*A*, case 5. There is a large hiatus in the underdeveloped radius at the site of fracture and subsequent infection. Because of the resultant shortening the ulnar head projects downward below the level of the carpometacarpal joints. *B*, case 6. Angulation has resulted in a foreshortening of the radius so that the ulnar head overlies the first row of carpal bones.

In addition there appeared to be a definite lateral bowing of the radius. The roentgenogram (fig. 5 *B*) disclosed angulation, rotation and slight upward displacement of the distal fragments of the fractured radius. This is the characteristic position of fracture occurring below the insertion of the pronator radii teres

and is probably due to the action of the pronator quadratus muscle. Simple refracture with bone suture was unsatisfactory, and the patient was ultimately subjected to bone graft operation.

By all means the most common cause of relative disproportion (shortening) of the radius is inadequate reduction in Colles' fracture. In large part, the unsatisfactory results obtained in the treatment of this most common type of fracture are due to failure to appreciate its complicated character. So much stress has been laid on the correction of the "silver fork" deformity that it has overshadowed the existence and necessity for treatment of other more important deformities. Foremost among these are supination of the distal fragments and relative shortening of the radius. While neglect of the former of these two deformities may lead to a persistence of an apparent dorsal prominence and some limitation of rotation, failure to correct the latter inevitably leads to weakness, pain and unsightly appearance of the wrist.

As in other conditions, the best form of therapy is prophylactic and consists in anatomic reduction of the fracture. In cases in which malunion has already taken place, definitive therapy will depend on the age at which the patient is seen. When epiphyseal growth is still possible, premature ossification of the lower part of the radial epiphysis necessarily forecasts progressive disproportion in the length of the bones of the forearm. In such circumstances, surgical ablation of the unaffected epiphyses will result in a shortening of the forearm and prevention of the disabling inequality characteristic of untreated patients.

For older patients in whom full maturity of the bone has been reached only two therapeutic possibilities exist: lengthening of the affected radius or shortening of the normal ulna. Lengthening of the radius, like the lengthening of other bones, is fraught with many difficulties. When successful, it represents a dramatic surgical triumph, but as a routine surgical practice shortening of the longer bone will be found more generally applicable.

This principle was first employed in 1927 in the following instance.

CASE 7.—Minnie T., aged 35, came to the hospital in 1927, eight years after fracture of the left wrist which followed a fall downstairs. She received no treatment at the time. During the past few years she had noticed gradually increasing pain which she attributed to "change of weather or washing clothes."

Examination disclosed notable prominence of the ulnar head on the dorsum of the wrist. The wrist was deviated to the radial side, and there was definite pain on pronation and supination of the forearm. On pronation the ulnar prominence became less noticeable. Supination was definitely limited by what seemed to be a bony impingement against the lower end of the ulna. The pre-operative roentgenogram (fig. 6) disclosed that the whole radiocarpal mass was displaced upward and anteriorly. The head of the ulna, projecting downward, lay on the dorsal surface of the cuneiform bone and during the act of supination acted as a bone block against the dorsum of the carpus. To overcome the



inequality in bone length a Z-shaped piece of bone, with shortening of the ulna, was resected on May 23, 1927. No metallic fixation was employed, and though only incomplete correction was obtained a definite improvement in function resulted.

Credit for the original effort in the treatment of this condition must be given to Darrach. In an article which appeared in the *Annals of Surgery* in 1913 Darrach advised resection of the projecting lower end of the ulna. This operation, which has gained wide recognition, is relatively simple to perform and readily eliminates the objectionable prominence of the ulnar head. It may, however, result in an unesthetic



Fig. 6 (case 7).—Preoperative anteroposterior and lateral views. The shortening of the radius, with anterior dislocation of the carpus and the ulnar head lying on the carpal cuneiform bone, is apparent.

widening of the wrist, arthritis of the radioulnar joint and, above all, a weakening of the wrist due to severance of the ulnar collateral ligaments at the wrist.

CASE 8.—Gloria S., aged 17, was first seen in November 1947. Some six years earlier she had fallen and injured her left wrist. The exact damage is unknown, but two years ago a resection of the lower end of the ulna was performed because of pain and interference with motion of the left wrist. For some time after this operation the patient noted an improvement in the function of the wrist. Recently she has begun to complain of pain and swelling of the wrist, with inability to use her left hand normally for writing.

Examination disclosed a small well healed scar over the lower end of the left ulna. Pronation and supination were only slightly impaired by pain but were associated with a definite clicking sensation. The patient complained of a sense of weakness and looseness in the wrist. This was confirmed by the hypermobility of the wrist and particularly of the lower end of the ulna, which could be easily displaced either backward or forward.

The roentgenogram (fig. 8) disclosed a definite malformation of the ulnar head, with hypertrophic arthritic changes at the distal radioulnar joint. To



Fig. 7 (case 7).—After Z-shaped resection of the ulna incomplete correction of the disproportion has been achieved.

strengthen the wrist the patient was fitted with a small protective apparatus. This is of purely palliative value, and it is feared that ultimately the development of painful arthritis may make further operation necessary.

It may be that both the widening of the wrist previously observed and the arthritis here noted are the consequences of technical imperfections. On the other hand, weakening of the wrist by detachment of the ulnar collateral ligaments seems to be unavoidable.

To overcome these defects a true shortening of the ulna in continuity rather than a resection of its distal portion has been suggested.<sup>8</sup> The operation is exceedingly simple from a technical point of view. An incision is made over the subcutaneous border of the ulna, and the shaft is exposed subperiosteally at a distance sufficiently above the tip of the ulna to permit the application of a small Lane plate. The portion of bone to be resected is just sufficient to bring the ulnar head to the level of the lesser sigmoid notch on the radius. The resection may be Z or V shaped or transverse, and thereafter the bone ends are fixed by means



Fig. 8 (case 8).—After resection, the lower end of the ulna is deformed. Arthritis of the inferior radioulnar joint has developed.

of a small four screw Lane plate. The wound is closed, and the extremity is immobilized from above the elbow until roentgenograms reveal bony union at the site of osteotomy.

This operation is technically somewhat more complicated than Dar-  
rach's operation but is not excessively trying either to the surgeon or  
to the patient. Occasionally nonunion of the ulna has been observed.  
It is believed that this is largely due to the fact that simple suture by

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8. Milch, H.: Cuff Resection of the Ulna for Mal-United Colles' Fracture, *J. Bone & Joint Surg.* **23**:311 (April) 1941; footnote 4.

wire or surgical gut has been employed. Since nonunion is in all probability the result of inadequate immobilization, it is suggested that internal plate fixation be employed. The merit of the method lies in the fact that it abolishes the disabling disproportion in length and eliminates the ulnar prominence without disturbing the anatomic structures which maintain stability of the wrist.

#### CONCLUSIONS

Attention has been directed to a varied group of cases in which the salient anatomic characteristic is a shortening of the radius. Normal function of the forearm is predicated on the maintenance of normal length relationships between radius and ulna. Shortening of the radius is clinically manifested by a "so-called dislocation of the ulna." This is a misnomer which should be discarded. Disparity in the length of the bones of the forearm should be corrected not by resection of the lower end but by actual shortening of the shaft of the ulna. This permits restoration of function without jeopardizing the stability of the wrist joint.

## USE OF SKIN GRAFTS IN REPAIR OF CLEFT PALATE TO IMPROVE SPEECH

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THE ULTIMATE aim of surgery of the cleft palate is not only to close the defect but to establish normal speech. In the latter objective surgical repair frequently fails, even after adequate periods of speech therapy. In many cases this is due to the anterior pull of the contracting raw surfaces on the nasal side of the mucoperiosteal flap, which results in a "short palate." When healing has occurred, the contracted scar tissue prevents the velum from closing the velopharyngeal sphincter, and so the patient's speech remains defective.

Many ingenious methods have been devised to overcome this fault in the von Langenbeck operation. Advancement of the pharyngeal wall has been advocated and has been effected by such methods as vertical suturing of a transverse incision,<sup>1</sup> formation of pharyngeal flaps,<sup>2</sup> injection of paraffin<sup>3</sup> and insertion of cartilage, but in general these procedures either do not remain effective or are actually harmful.

The concept of lengthening the palate rests on a practical basis, and numerous operations using flaps from the palate, posterior pillars and buccal mucosa and even extraoral flaps have been proposed. Some of these procedures are formidable, others are time consuming and a few result in a high percentage of failures.

Gillies<sup>4</sup> in 1921 reported a method of applying a skin graft to the anterior raw surface of the soft palate after it had been retrodisplaced. The resulting anterior defect in the hard palate he corrected by means of an obturator. Dorrance<sup>5</sup> has termed the obturator "an affront to the surgical mind," and we are in complete agreement with this state-

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ment. Anyone who has had experience with growing children and with obturators which must be enlarged yearly realizes that any method which closes the palate completely is preferable to condemning the patient to "obturator life."

In an effort to overcome this difficulty, cleft palates were created surgically on dogs in the Experimental Surgical Laboratories of McGill University in 1940, and experiments were performed to see if grafts of the dogs' oral mucosa could be successfully grown on the nasal side of the mucoperiosteal flaps. This was discovered to be feasible, and in 1941 the method was applied to patients with various types of cleft palate, skin from a hairless area of the body being used.

During the past six years the advantages and some of the technical difficulties of applying skin grafts to the palate have been observed.

The essential principle involved is that of applying an epithelial covering to the raw surface on the nasal side of the mucoperiosteal flap. After the mucoperiosteal flap has been dissected back to the junction of the bony palate and the aponeurosis of the soft palate, dental compound is carefully molded to the space between the hard palate and the mucoperiosteal flap to form a stent. The contour of the stent is oval on cross section, and it should be trimmed until it is somewhat smaller than the cavity into which it will be inserted, so that when the flap is replaced the margins of the wound can be approximated without tension. A split skin graft taken from a hairless part of the body is wrapped, raw surfaces outward, about the compound stent, and the edges are sutured. It is advantageous to use the stent because it serves to keep the skin graft in close contact with every irregularity of the bony palate and mucoperiosteal flap. In addition the skin graft is prevented from contracting until the stent has been removed.

In the usual sequence, "the set-back" procedure is carried out two or three weeks after the application of the skin graft. Formerly it was considered necessary to sever the greater palatine arteries to allow the flap to be sufficiently retrodisplaced, but it has been found in the majority of cases that it is possible to stretch the arteries and veins out of the pterygopalatine canal for a considerable distance, sufficient to make their cutting unnecessary. Occasionally it is necessary to remove part of the posterior wall of the canal and the palatine foramen to avoid kinking of the vessels and to permit the palate to be set back freely, as described by Brown. When removing the bony wall with a chisel, it is most important to avoid damaging the vessels or constricting the artery by compressing the contents of the canal. In a recent case we observed the blanching of the palate, which was considered to be due to vasospasm. This subsided gradually, and no injury to the palate resulted. When this stage of the operation is being performed it is imperative that the skin graft be trimmed away from the margins of

the palatal flap so as to provide a sufficient raw area for union with the posterior part of the palatal bone. The tip of the flap should be securely fixed with wire or dermal sutures to prevent it creeping forward; these sutures should be left in place for several weeks. If the lateral edges of the flap cannot be approximated with sutures, it may be necessary to apply a wire cribwork or an acrylic splint to the teeth to insure primary

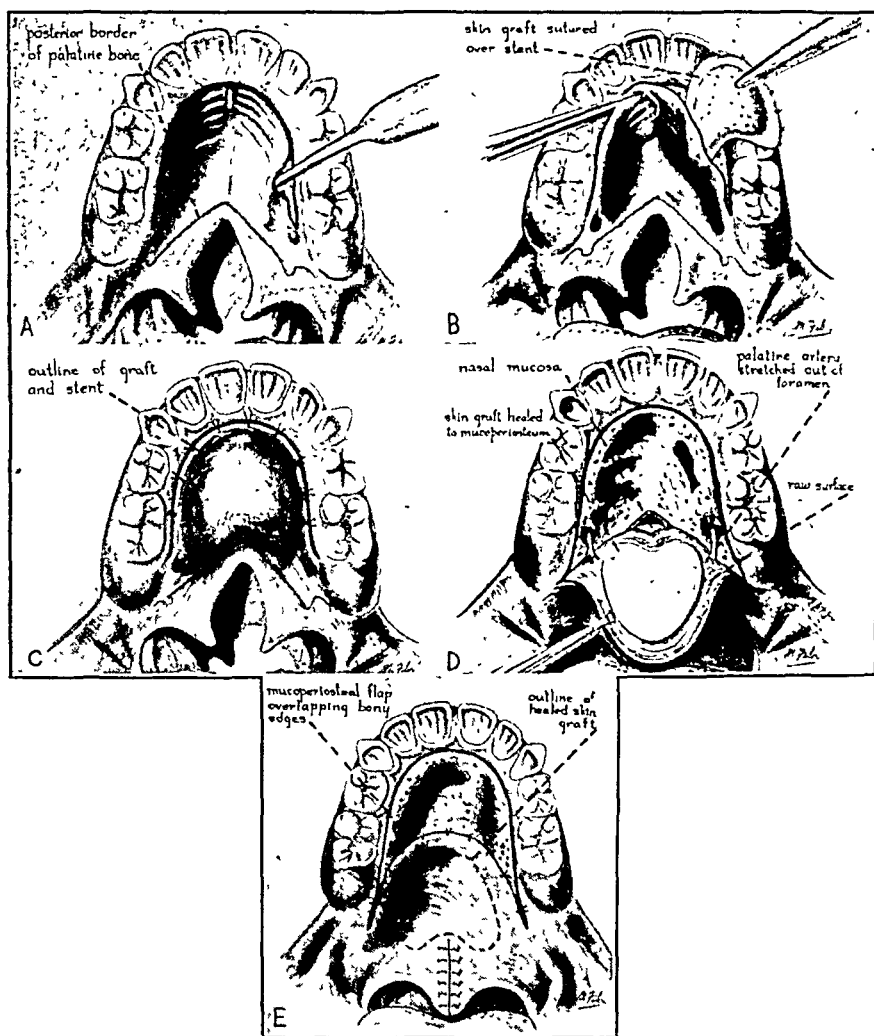


Fig. 1.—*A*, elevation of mucoperiosteal flap, through a U-shaped incision. *B*, insertion of skin graft-covered stent beneath mucoperiosteal flap. *C*, mucoperiosteal flap sutured over stent. *D*, mucoperiosteal flap raised with attached skin graft preparatory to "set-back" operation. The skin graft attached to the palatal bone has been removed. *E*, the retrodisplaced palate flap has been sutured to the posterior border of the palatal bone and the cleft in the palate has been repaired.

union of the edges of the flap. The palatal cleft is closed in the usual manner at the same time that the retrodisplacement procedure is carried out. Palatal massage begun four to six weeks after operation is helpful in mobilizing the palate.

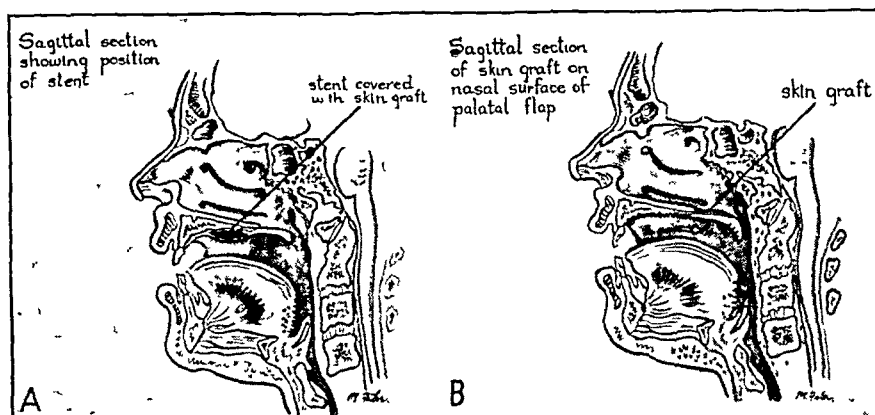


Fig. 2.—*A*, preoperative position of stent. *B*, postoperative position of skin graft-lined flap.

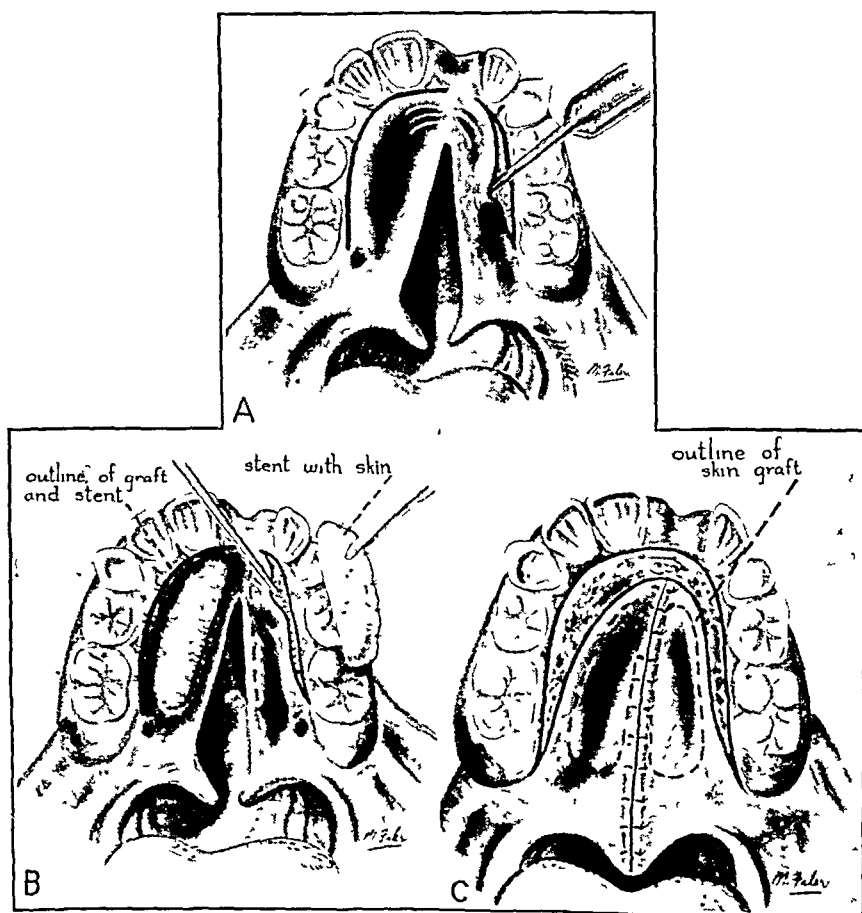


Fig. 3.—*A*, type of incision employed when cleft extends to alveolar ridge. *B*, two skin graft-covered stents are inserted, one on each side of the cleft. *C*, postoperative position of the flap.



## METHODS

I. *Congenital Short Palate, Cleft of the Soft Palate and Cleft of the Soft Palate and Part of the Hard Palate.*—In these three types of palatal defect the same method of operation may be employed. A U-shaped incision is made from the molar region of one side around to the opposite molar tooth, about three or four millimeters lingual to the teeth. The mucoperiosteal flap is raised and freed

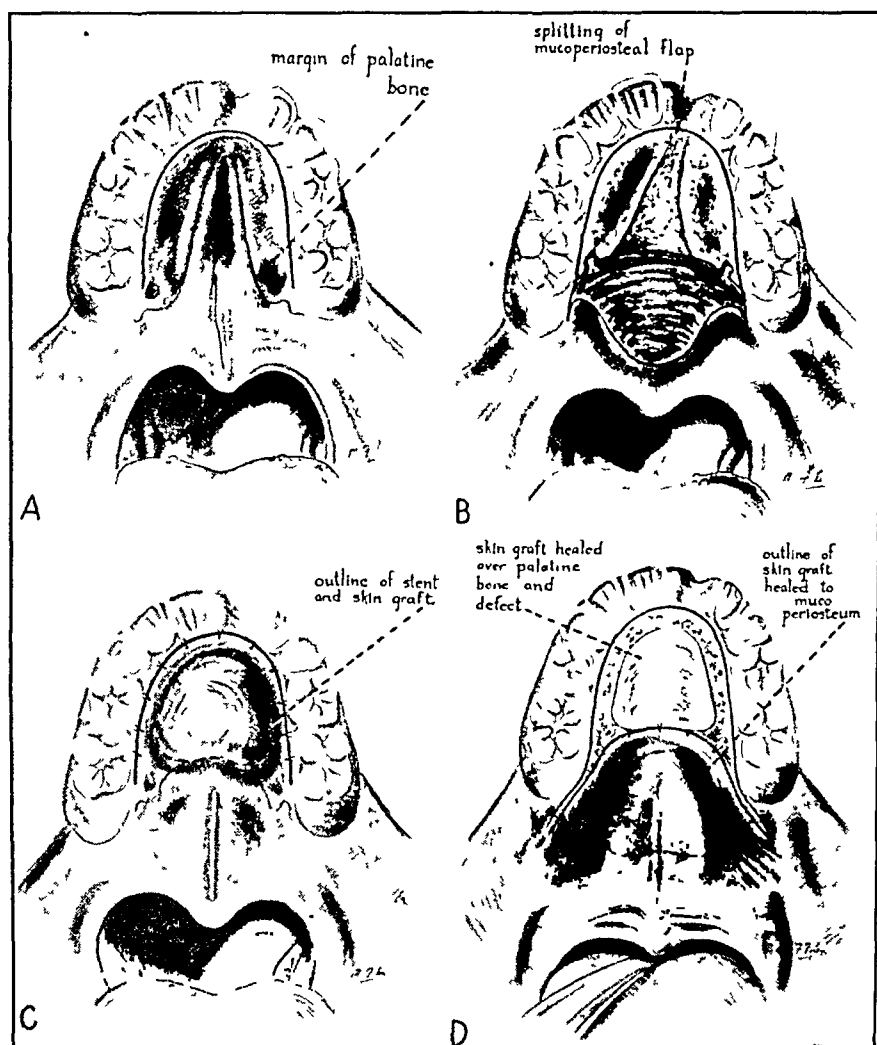


Fig. 4.—A, type of incision employed when a short, contracted palate is present after primary repair. B, splitting of the mucoperiosteal flap without perforation into the nasal cavity. C, mucoperiosteal flap resutured over stent graft. D, "set-back" of skin graft-lined flap.

posteriorly as far as the greater palatine arteries and the aponeurosis of the soft palate. Dental compound is shaped to fit the cavity and is trimmed so that the mucoperiosteal flap can be easily approximated over it, allowing for the thickness of the skin graft. The stent is covered with the skin graft, raw surface outward, and is placed beneath the flap, which is sutured over it. Two or three

weeks later the flap is again raised through the original incision line, the stent is removed and the skin graft which has united with the bony palate is stripped off, without injuring the graft on the mucoperiosteal flap. The incision is continued around the tuberosities of the maxilla and some distance posteriorly, the hamular processes divided, the aponeurosis separated from the palatal bone and the vessels carefully stretched out of the posterior palatine canal and freed from the palatal flap as much as possible. If necessary, the posterior walls of the palatine foramens may be carefully cut away with a chisel. The tip of the retrodisplaced flap is sutured with wire or dermal sutures so that it overlaps the posterior border of the hard palate sufficiently to permit solid healing without a perforation occurring (figs. 1 and 2).

II. *Cleft of the Hard and Soft Palate Extending to the Alveolar Ridge.*—In this type of cleft the vomer is frequently rudimentary. As before, an incision is made close to the gingival margin and carried posteriorly as far as the greater palatine foramens. The flaps are raised as shown in figure 3A, and in this case two stents are made, one for each side. They are covered with the split skin grafts, raw surface outward, and placed under the flap, one on either side of the cleft. Two or three weeks later the flaps are again raised, the incisions joined anteriorly, the stents removed and the incisions extended posteriorly as before. The skin grafts on the palatal bone are stripped off, the vessels gently stretched out of the posterior palatine foramens and the hamular processes fractured. The palatal flap is displaced posteriorly so that its tip approximates the anterior end of the bony defect and is sutured in position. The cleft is closed in the usual manner. In this type of cleft the retrodisplacement is not as extensive, but the presence of skin grafts on the nasal side of the flaps minimizes the amount of postoperative contracture.

III. *Bilateral Complete Cleft Palate.*—The method described by Dorrance of reflecting flaps of mucous membrane bilaterally from the vomer to close the anterior part of the defect is satisfactory. After the anterior portion has filled in with granulations, mucoperiosteal flaps may be raised, lined with skin grafts and subsequently retrodisplaced (fig. 3).

IV. *Secondary Repairs.*—One of the major problems in surgery of the cleft palate is the patient who has had a single or double cleft repaired by the Langenbeck procedure yet whose speech remains defective because of the short contracted palate. In these patients a "push back" may fail to accomplish the desired speech result because of contracting scar tissue on the nasal side of the flap. In selected cases it may be possible to split the mucoperiosteum without penetrating the nasal side and insert a skin-covered stent and later to retrodisplace the flap in the same manner as that described in method no. 1 (fig. 4).

#### REPORT OF CASES

The following cases illustrate the method of treatment of various types of palatal defects and the results which have been obtained.

CASE 1.—J. M., aged 6 years, with an intelligence quotient of 82 (normal, 100), had a congenital short palate.

*Preoperative Examination.*—Cleft palate type of speech was present. The plosives, sibilants and fricatives were all lost, with glottal substitution.

*Operations.*—1. A stent skin graft was applied to the mucoperiosteal flap. 2. A "set-back" of the palatal flap was performed, and the major palatine arteries were saved. Note extent of the set-back from A and B.

*Postoperative Examination.*—After a course of speech therapy, a test showed that the patient's speech was perfect except that the "S" had changed from a glottal stop to a dental lisp (fig. 5).

*Nasopharyngoscopic Examination.*—The outline of the skin graft to the nasal aspect of the mucoperiosteal flap was easily observed. A considerable degree of metaplasia had occurred, and the graft was pinkish and appeared to be soft and flexible.

CASE 2.—M. F., aged 13 years, with an intelligence quotient of 109, had cleft of the soft palate and half of the hard palate (fig. 6A).



Fig. 5.—Postoperative results, showing marked amount of retrodisplacement of mucoperiosteal flap obtained.

*Preoperative Examination:* There was a general nasal blur on all vowels. The worst consonants were the sibilants. Nasal grimaces accompanied all these sounds.

*Operations.*—1. A stent skin graft was applied to the mucoperiosteal flap. 2. "Set-back" of the palate and closure of the cleft were accomplished. The major palatine arteries were saved (fig. 6B). 3. Repair of the small hole in the palate (fig. 6C and D) was carried out.

*Postoperative Examination.*—At the end of the course of therapy the patient's speech was entirely normal. The only remaining evidence of the facial grimaces was slight nasal twitch on sounding "S."

*Nasopharyngoscopic Examination* (November 1946).—The skin graft was smooth and flexible and was beginning to undergo metaplasia.

CASE 3.—D. C., aged 6 years, had an intelligence quotient of 100. The diagnosis was cleft of the soft palate and half of the hard palate (fig. 7A).

*Preoperative Examination.*—Cleft palate type of speech was present. The plosives, sibilants and fricatives were all lost, with glottal substitutes.

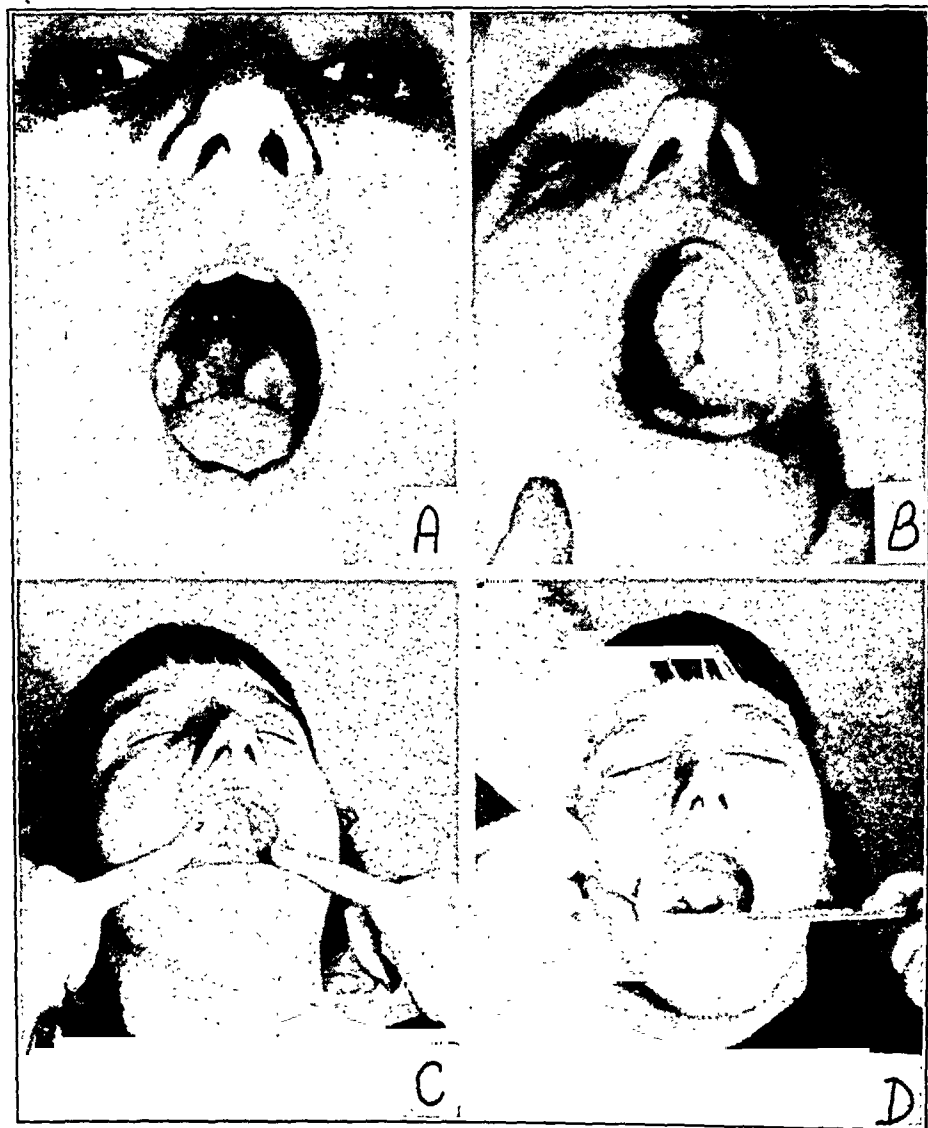


Fig. 6.—A, wide cleft of soft palate and half of hard palate with rudimentary vomer, shown preoperatively. B, small hole at junction of hard and soft palate, probably caused by inclusion of a piece of skin graft in suture line, which required secondary repair. C, showing palate smoothed out and repair of small perforation. D, long, mobile soft palate one year postoperatively.

*Operations.*—1. A stent skin graft was applied to the mucoperiosteal graft. 2. "Set-back" of the palate and closure of the cleft were accomplished. The major palatine arteries were saved (fig. 7B).

*Postoperative Examination.*—The patient is attending a speech clinic. All consonants were articulated perfectly. Some nasal resonance was present on vowels, and there was a low "S."

*Nasopharyngoscopic Examination* (November 1946).—The skin graft was white and smooth, and no raw areas were visible.

CASE 4.—D. W., aged 13 years, had an intelligence quotient of 100. The diagnosis was previous complete cleft lip and palate on the left side. The lip and palate had been repaired, but the latter was short, and there was a hole in the soft palate. The patient was referred for repair (fig. 8A).

*Preoperative Examination.*—There was over-all general nasal resonance on vowels. The plosives were distorted, with glottal substitutions, and the sibilants and fricatives were glottalized.



Fig. 7.—A, cleft of palate preoperatively. B, retrodisplaced skin-grafted flap one month postoperatively, before it had smoothed out completely.

*Operations.*—1. Stent skin grafts were used to line the mucoperiosteal flaps. The Wardill incision was used anteriorly, while on the posterior half of the hard palate the mucoperiosteal flap was split by the method described by Dr. James B. Brown. 2. Since the major palatine arteries had been severed by the previous operator, a "push-back" of the palate was performed. At the same time the hole in the soft palate was repaired (fig. 8B).

*Postoperative Examination.*—One month after the last operation the patient was admitted to the speech clinic. A test at the time showed that all consonants were articulated perfectly. There was nasal resonance on all vowels, with a velar "K" and "G" and a low "S." The palate was long, and a good speech result was anticipated.

*Nasopharyngoscopic Examination* (November 1946).—The grafted area appeared as a moist, opaque, white area. There was no crusting, and no raw areas were visible.

CASE 5.—A. W., aged 26 years, had an intelligence quotient of 90.

*Diagnosis.*—As a result of diphtheria when the patient was 9 years old the uvula and part of the soft palate had sloughed, with extensive residual scarring (fig. 9A).

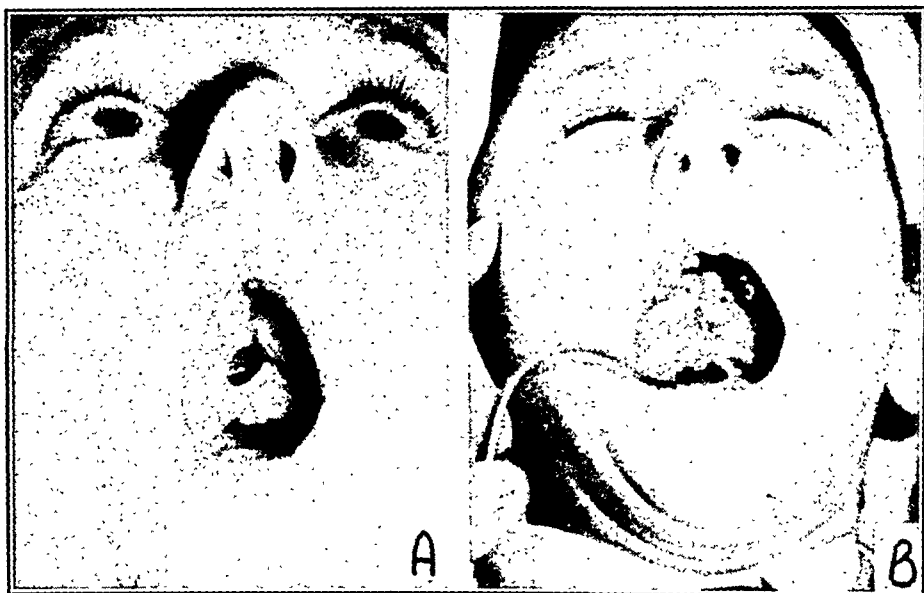


Fig. 8.—A, this patient was referred to the clinic for treatment. The previous operator had obtained a short, tight palate with a large perforation in the soft palate. B, photograph taken a few weeks after the final operation, showing the amount of displacement backward and closure of the perforation.



Fig. 9.—A, this patient survived an attack of diphtheria as a child but suffered extensive sloughing and scarring of the soft palate. B, the tip of the mucoperiosteal flap is shown overlapping the posterior border of the hard palate by only a few millimeters. The patient wears a full denture with comfort.

*Preoperative Examination*—There were glottal substitutions for the plosives, and there was nasal resonance on all vowels. The sibilants were nasalized.

*Operations.*—1. Ligation of major palatine arteries was carried out. 2. A stent skin graft was applied to the mucoperiosteal flap. 3. "Push-back" of the palate flap was performed.

*Postoperative Examination.*—The patient was unable to attend the speech clinic. Five years after operation the sounding of all consonants was good, although there was some nasal resonance on the vowels. A course of speech therapy is now being given to correct this slight residual defect (fig. 9B).

*Nasopharyngoscopic Examination* (November 1946).—The skin graft could be differentiated from its surrounding mucosa only by a pale whitish tinge.

*NOTE.*—Because of the pressure of a full upper denture which the patient has been using for the past five years and perhaps because of a process of metaplasia, it

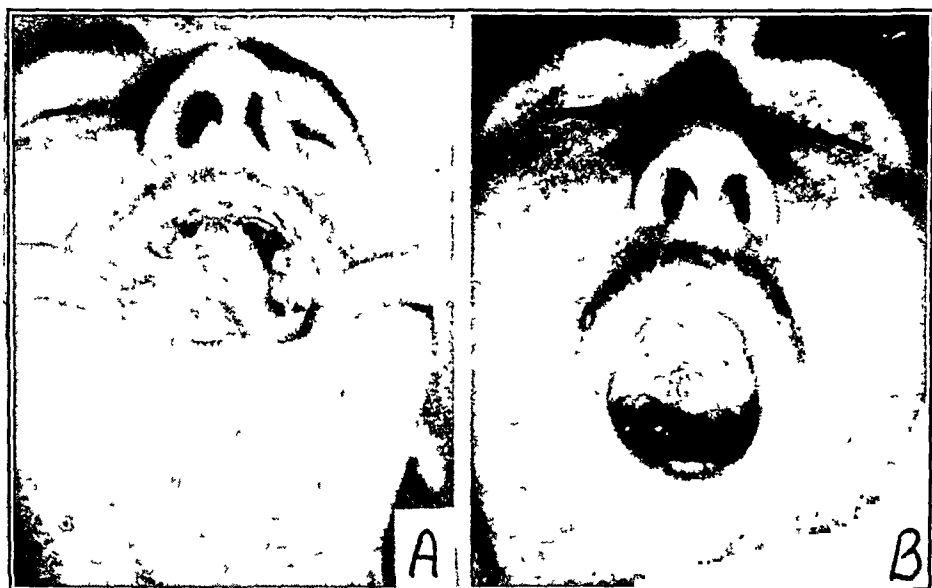


Fig. 10—Long, noncontracting palate obtained after skin grafting and closure of cleft which extended almost to the alveolar ridge. Two previous operations, with complete failure, had been performed on this patient

was difficult to recognize the presence of the skin graft which had been applied to the oral surface of the hard palate, and which in this case was not removed.

#### SUMMARY

Skin grafts have been applied to the nasal aspect of the mucoperiosteal flaps in 22 patients. The skin grafts failed to take in only 3 cases, and in these the operation was successfully completed by a second skin-grafting procedure. Now we use sodium penicillin in isotonic sodium chloride solution, 25,000 units per cubic centimeter injected about the stent and skin graft, before suturing the flap back into position, and in patients in which this has been used there have been no infections. Primary union occurred after closure of the clefts in all except 1 case,

in which a tiny hole 2 mm. in diameter remained, probably owing to inclusion of a small piece of skin graft in the suture line when the cleft was closed. In 2 patients the mucoperiosteal flaps failed to unite primarily at their lateral margins, possibly because of failure to trim the skin graft sufficiently from the margins of the flap. Secure fixation of the flap to obtain close contact of the margins by means of suture, wire crib or acrylic splint is important.

The application of a skin graft to the raw surface on the nasal aspect of a mucoperiosteal flap in selected types of palatal defects appears to be a satisfactory procedure, both theoretically and practically, as far as can be determined from a limited number of cases.

In all patients examined with the nasopharyngoscope the graft was found to be viable and there was no evidence of crusting or offensive odor. Grafts over a year old had assumed a pinkish color, and one graft over five years old had apparently undergone considerable metaplasia, for only a faint whitish tinge differentiated it from the surrounding mucosa.

Some technical complications have been noted after this type of operation, and measures to reduce their incidence have been described.

The results obtained after this procedure for correction of cleft palate and the usual period of speech training were definitely better than those observed after the ordinary type of repair.

This operative method requires an extra stage, and we realize that it is essential to perform each step with painstaking exactitude, for any carelessness or short cuts may jeopardize the success of the whole procedure. However, we believe that this additional care is worth while because we have seen a considerable number of patients who appeared to have long, loose palates after a successful "set-back" or "push-back" operation and in whom, after a few months, so much contracture of the palate developed anteriorly as a result of scar contracture of the raw surface on the nasal side of the palatal flap that even prolonged therapy could not improve their speech. Indeed, a number of these patients have been greatly improved after a subsequent skin-grafting operation.



## CONTUSIONS OF THE LUNG FROM NONPENETRATING INJURIES TO THE THORAX

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THE LUNG is subject to damage from nonpenetrating injuries to the thorax. The more severe injuries to the lung, with hemothorax and pneumothorax, have been repeatedly stressed in the literature,<sup>1</sup> but the minor degrees of injury resulting in contusion have received little attention. In an army hospital receiving patients with combat injuries from the army air forces all gradations of injury from contusion to rupture of the lung from nonpenetrating injuries were seen. The agents responsible for the changes in the lung were blast from high explosive shells, blows from blunt objects and nonpenetrating wounds caused by high velocity missiles. Of particular interest, and the subject of this report, were the rapidly clearing areas of pulmonary consolidation noted in some of the cases of injury to the thoracic wall.

Blast injuries to the chest from high explosives have been emphasized in the past war.<sup>2</sup> The accepted explanation for the pulmonary injury caused by blast is the presence of a high positive pressure wave that compresses the chest and abdomen not only by the marked increased pressure but by the force of the wave traveling at tremendous speed. This, then, acts as a blow to the thorax as from a large blunt object. Among the factors that influence the severity of the lesion produced are the amount of padding on the thoracic wall, the position of the chest in relation to the direction of the explosion and the flexibility of the wall. The cases (table 1) reported in the series were from a group of air force personnel exposed to the explosion of approximately 10,000 pounds (4,535 Kg.) of high explosive bombs. Of the 39 patients exposed to the blast requiring hospitalization, 19 had hemoptysis and 9 of these had roentgenologic evidence of pulmonary contusion, 1 had hemothorax

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2. Zukerman, S.: Experimental Study of Blast Injuries to the Lungs, *Lancet* **2**:219, 1940.

and cardiac arrhythmia and another had pneumothorax. These patients were all admitted to the hospital within six to eight hours after injury.

Blows to the thoracic wall from blunt objects can cause notable compression of the thorax and result in contusion of the lung, just as in blast injuries.<sup>3</sup> The lung is suddenly compressed by the diminution in the size of the thorax, and the force is transmitted to the lung by its continuity with the wall of the chest. The injured lung in this series was adjacent to the contused wall. There are reports<sup>4</sup> of contra-coup injuries to the lung, most commonly in the posterior portion adjacent to the spine, as well as of injury to the opposite lung. When the chest is injured from blows received in a fast-moving surface vehicle or plane, the absence or presence of contra-coup injuries is hard to determine because of the inability to get a clearcut history of the injury. In none of the cases of simple contusion was there evidence of contra-coup injuries. Table 1 shows a list of the cases in this group studied. The pulmonary changes varied from contusions to rupture of the lung with

TABLE 1.—*Summary of Cases of Nonpenetrating Injuries of the Chest*

	No. of Cases	Hemop- tysis	Contusions of Lung	Hemo- thorax	Pneumo- thorax	Fractured Ribs
Blast injuries of the lungs...	19	19	9	1	1	0
Wounds of the thorax from nonpenetrating high explo- sive shell fragments.....	5	3	5	0	0	0
Blows to the thorax from blunt objects.....	16	13	16	7	7	10

hemothorax and pneumothorax. It is of interest that in 1 case without fracture of the ribs hemopneumothorax was present.

High velocity missiles wounding the thoracic wall but not penetrating the pleura may cause injury to the lung by the impact against the wall as well as by the high positive pressure wave that accompanies the missile. Daniel<sup>5</sup> demonstrated in dogs that wounds passing tangential to the chest caused greater injuries than did missiles passing through the lung. He postulated that this was caused by the high pressure wave adjacent to the traveling projectile. Contusion of the underlying lung from this cause was noted in 5 cases presented in this series.

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Fractured ribs accompanying the injury to the lung were not always present. In none of the cases with contusion of the lung caused by blast and high velocity shell fragments were there any fractured ribs. In 10 of the 16 cases of contusion of the lung from direct blows fractured

TABLE 2.—*Contusion of the Lungs*

Case	Cause of Injury	Hemoptysis	Röntgenologic Changes in the Chest	Duration of Röntgenologic Changes in the Lung, Days
1	Wound from high velocity shell fragment	Yes, 14 days	Area of consolidation of right mid-pulmonary field	17
2	Wound from high velocity shell fragment	Yes, 2 days	Area of consolidation from hilus to axilla in left upper pulmonary field	3
3	Wound from high velocity shell fragment	No	Area of consolidation at base of right lung	7
4	Wound from high velocity shell fragment	No	Area of consolidation at base of right lung	7
5	Wound from high velocity shell fragment	Yes, 1 day	Area of increased density at lateral aspect of base of right lung	7
6	Large spent shell fragment	No	Area of consolidation of right upper pulmonary field	6
7	Airplane crash	Yes, 2 days	Area of consolidation of both upper pulmonary fields; fracture of ribs 4 and 5 on left and ribs 1, 2, 3, 4 and 5 on right	7
8	Airplane crash	Yes, 3 days	Area of consolidation of both lower pulmonary fields	4
9	Struck in chest with airplane propeller	Yes, 11 days	Hemothorax on right side with consolidated area at base; area of consolidation in left hilar region; multiple fractures of ribs 7, 8, 9, 10 and 11 on left and ribs 9, 10 and 11 on right	11; left residual scar in right lower pulmonary field
10	Hlt in right lateral region of the chest in airplane crash	Yes, 2 days	Consolidation of right lower pulmonary field	4
11	Automobile accident	Yes, 1 day	Consolidation of lateral aspect of right lung	8
12	Airplane crash	No	Diffuse mottling of left hilar region beneath fracture of posterior part of left 5th and 6th ribs	8
13	15 feet (457 cm.) from explosion of 10,000 lb. of high explosives	Yes, 3 days	Diffuse areas of consolidation about both hilar regions	5
14	20 feet (609 cm.) from explosion of 10,000 lb. of high explosives	Yes, 2 days	Discrete areas of density of entire left lung and lower half of right lung	5

ribs were present. If the ribs are sufficiently elastic, the lung can be compressed without a break in the costal cage. Some observers<sup>3</sup> have pointed out that in the minor degrees of injury a fractured rib may break the force of the trauma before severe compression of the chest takes place. Of course, in cases of severe trauma of the chest the rib ends may be driven into the lung.

The three types of nonpenetrating trauma to the chest, then, all cause injury to the lung in the same manner: (1) by compression of the semiflexible thoracic wall, (2) by the transmission of the force to the underlying lung by the tissues of the thoracic wall and (3) occasionally by the driving into the lung of fractured ribs. Severe compression of the thorax may result in rupture of the lung and the parietal pleura, with hemothorax or pneumothorax, while less severe trauma

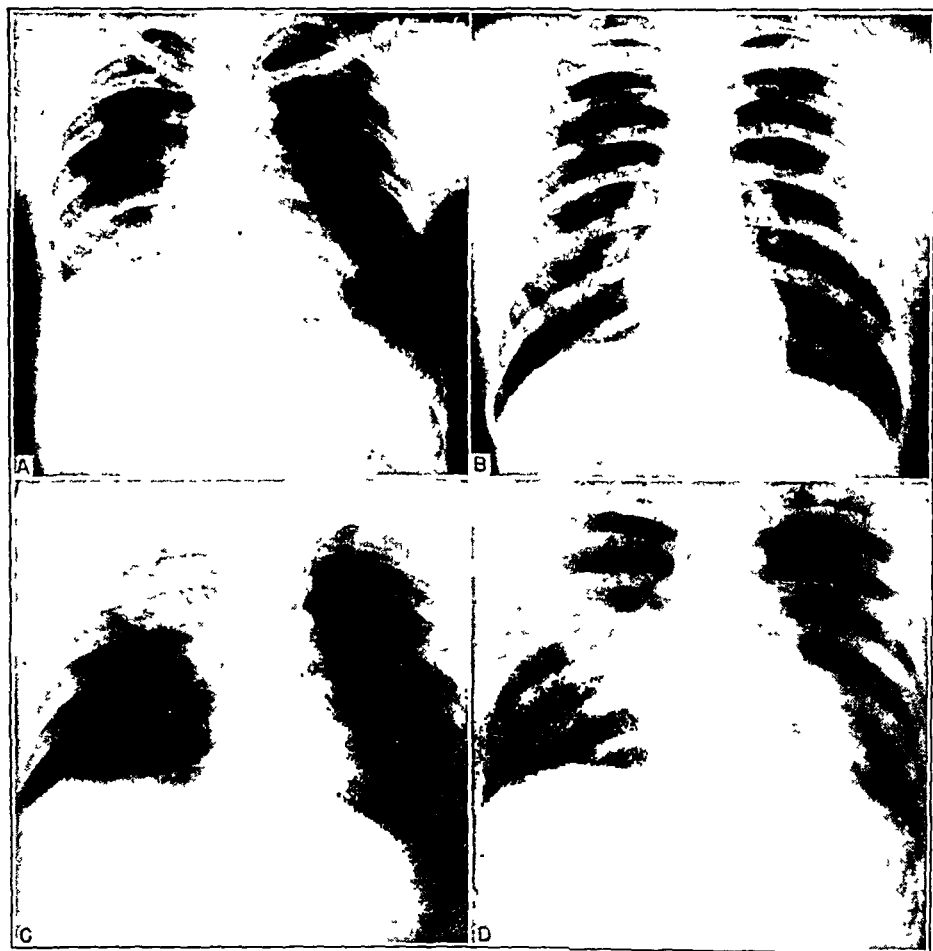


Fig. 1.—*A* (case 3, table 2), roentgenogram on admission of patient with contusion of right lower pulmonary field from high velocity shell fragment in the right lower region of the chest that did not penetrate the pleura. *B*, lung of same patient thirty days later. *C* (case 6, table 2), roentgenogram of patient with contusion of the right upper pulmonary field from blow to anterior region of chest from spent shell fragment. *D* (case 1, table 2), roentgenogram of patient with contusion of the right midpulmonary field from wound caused by high velocity shell fragment that did not penetrate the pleura

causes only rupture of the pulmonary parenchyma, the latter giving the picture of consolidation on roentgenograms. These areas of consolidation were seen in 14 cases and are recorded in table 2. In 7 cases

they were due to blows to the thoracic wall, in 5 to nonpenetrating wounds caused by shell fragments and in 2 to injury from a high explosive concussion blast. The areas varied in size, as shown in figures 1 and 2. In the cases of direct blows and wounds from high velocity shell fragments, the area of consolidation was adjacent to the injury of the thoracic wall. In a like manner the contusions from the effects of blast were noted in the lung nearest the explosion. In 1 of the 15 cases

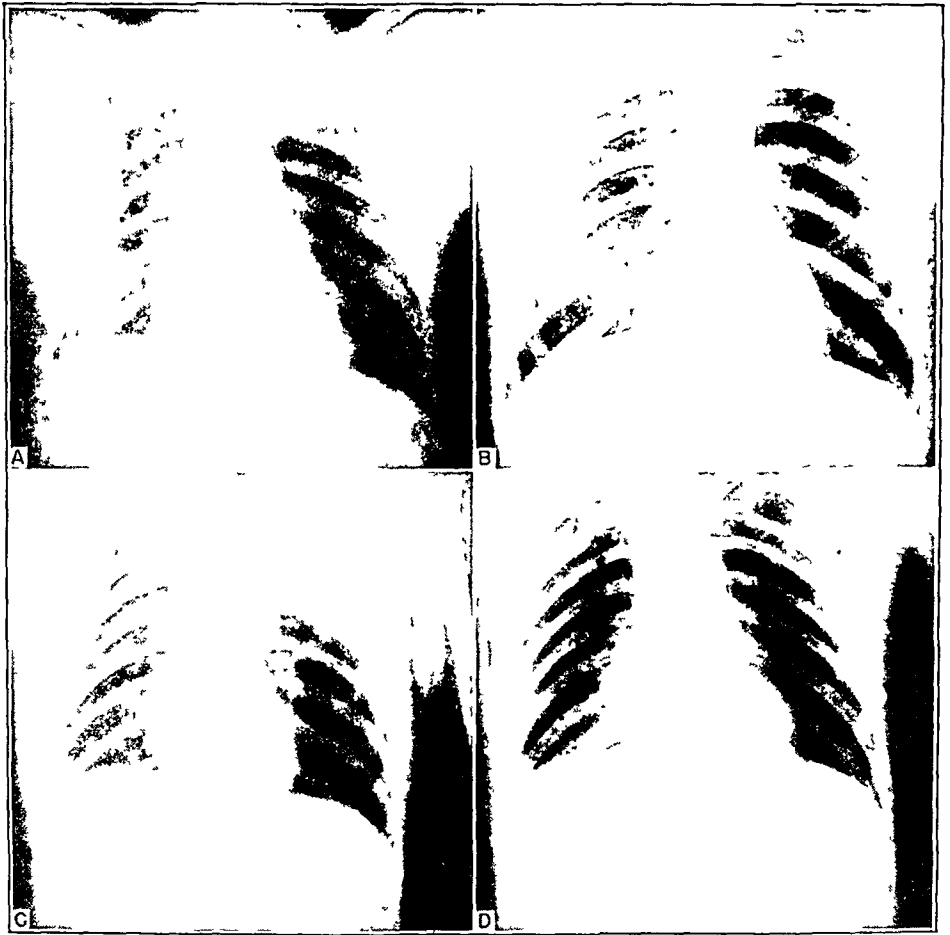


Fig. 2.—*A* (case 10, table 2), roentgenogram on admission of patient with contusion of the right lateral lower pulmonary field from blow caused by blunt force. *B*, lungs of same patient four days later. *C* (case 8, table 2) roentgenogram on admission of patient with contusion of both upper pulmonary fields from injury in airplane crash. *D*, lungs of same patient seven days later.

atelectasis developed in the lower lobe but the area of contusion was in the upper lobe. All patients received prophylactic doses of sulfadiazine and penicillin, and in no cases did pneumonia develop.

Hemoptysis was a prominent symptom in all the cases except 1. In some of the cases there was merely blood-tinged frothy material, while

in others there were frank clots. It is suggested that the multiple areas of increased density seen in some of the cases of blast and the "traumatic wet lung" might be due to flooding of the bronchial tree with blood. The other symptoms were inconstant and were dyspnea, pain in the chest and cough.

The areas of consolidation in the lung demonstrable on roentgenograms were interesting and significant in that they subsided rapidly, the average duration being six days. In some cases the consolidated areas were barely discernible in forty-eight hours. Because of this rapid clearing, it seemed most likely that the density apparent on the roentgenograms was as much the result of edema as of hemorrhage.

As the injuries from blows to the thoracic wall were not peculiar to war conditions, contusion of the lung may occur in civilian practice with more frequency than is generally recognized. A recent report<sup>6</sup> from an industrial plant emphasized the high incidence of lobar pneumonia in workers receiving blows to the thoracic wall. In all the cases presented in this study prophylactic doses of sulfadiazine and penicillin were administered and in none did pulmonary infection develop.

#### SUMMARY AND CONCLUSIONS

1. The lung may be injured in the intact thorax from any force that compresses the thoracic cavity or which is transmitted to the lung by continuity of tissue.

2. Injuries from the blast wave of an explosion, blows from blunt objects and wounds from high velocity missiles act on the thorax in essentially the same manner.

3. The changes in the roentgenograms of the lungs with the minor degree of injuries are due to contusion of parenchyma followed by edema and hemorrhage.

4. The rapidity of the resolution of the contusion of the lung suggests that the occurrence is more common than is generally recognized.

5. Hemoptysis was the commonest symptom in the cases presented.

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6. Phillips, E.: Pneumonia Following Non-Penetrating Pulmonary Injuries, *J. A. M. A.* **133**:161 (Jan. 18) 1947.

## TECHNIC FOR ARTHRODESIS OF THE HIP WHEN THE FEMORAL HEAD AND NECK ARE ABSENT

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ARTHRODESIS of the hip joint when the femoral head has been removed or when there is nonunion of the femoral neck with a necrotic head presents certain difficulties not present in other circumstances. The chief of these is in maintaining the trochanter in the freshened acetabulum without placing the lower extremity in too much abduction. Another is in obtaining enough bony contact between the femur and the ilium to assure fusion without an unduly prolonged period of immobilization. Since the upper end of the trochanter is rather small, there is more difficulty placing grafts to good advantage than when the head and neck are present. In the technic to be described, these difficulties have been satisfactorily overcome.

During World War II, a considerable number of patients were seen who had been struck in the hip by a high velocity missile which shattered the neck of the femur. Infection of the wound often followed, and the femoral head and fragments of neck were removed as sequestrums. If infection did not occur, aseptic necrosis of the femoral head, with nonunion, developed in a rather large percentage.

On examination these patients had an average of  $1\frac{1}{2}$  to  $2\frac{1}{2}$  inches (3.8 to 6.3 cm.) of shortening of the affected extremity due to upward shift at the hip joint. None of our patients was able to walk without crutches or an ischial-bearing brace because of pain and instability in the hip. All had been completely free of drainage for at least five months before a definitive operation was considered.

The choice of procedure seemed to lie between some type of trochanteric arthroplasty and arthrodesis. In the 7 cases on which this article is based arthrodesis was chosen for the following reasons:

1. All the patients had had an infection in the hip rather recently. (The shortest time to elapse between cessation of drainage and arthrodesis was five and a half months and the longest time fifteen months.)

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It was believed that the surest way to prevent further trouble from infection was to eliminate motion.

2. All were young men and desirous of a strong pain-free hip which would permit as much activity as possible with a minimum likelihood of further hospitalizations.

3. All had a normal hip on the opposite side, and the lumbar region of the spine was normal.

These patients had been allowed up on crutches, in some cases even before drainage had stopped. This improved their general condition, and since some motion occurred in the hip, it was a fair test of the dormancy of the infection. Physical therapy was given to get the knee and ankle on the affected side as nearly normal as possible before being subjected to another period of immobilization.

#### OPERATIVE TECHNIC

The patient is placed on a fracture table, with a sand bag under the affected hip. A transfusion of whole blood is started at the time the incision is made and continued throughout the operation, an average of 1,000 cc. being used.

The exposure is obtained by a Smith-Petersen incision,<sup>1</sup> the distal limb of which curves laterally about an inch and a half (3.8 cm.). The anterior portions of the gluteus medius and gluteus minimus muscles and the origin of the tensor fasciae latae are stripped from the lateral surface of the ilium. The space between the tensor fasciae latae and the rectus femoris muscle is located and the incision carried down between these muscles. Then the line of cleavage between the vastus lateralis muscle and the rectus femoris is found, and this is the plane of incision down to the upper end of the shaft of the femur. It is necessary to cut through the upper ends of the origin of the vastus medialis and vastus intermedius muscles.

The sartorius muscle is detached from the anterior-superior region of the spine, the abdominal muscles detached from the iliac crest and the iliacus muscle stripped from the inner aspect of the ilium down to the iliopectineal line. Both heads of the rectus femoris are detached (fig. 1).

The entire upper end of the femur is completely stripped down to the lowest point of the lesser trochanter. The muscle insertions at the tip of the greater trochanter are most easily detached with a sharp osteotome, care being taken to preserve the firm cortex. The leg is then adducted and externally rotated, the upper end of the femur being

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1. Smith-Petersen, M. N.: Treatment of *Malum Coxae Senilis*, Old Slipped Upper Femoral Epiphysis, Intrapelvic Protrusion of the Acetabulum, and *Coxa Plana* by Means of Acetabuloplasty, *J. Bone & Joint Surg.* **18**:869-880. (Oct.) 1936.



swung out of the wound, exposing the acetabulum, which is filled with scar or a necrotic head. All scar and cartilage is completely excised down to fresh bleeding bone, including the transverse ligament which bridges the acetabular notch. This is an important step because, unless everything is removed from the inferior portion of the acetabulum, difficulty will be experienced later in getting the shaft over far enough medially. A notch is then made in the upper outer portion of the

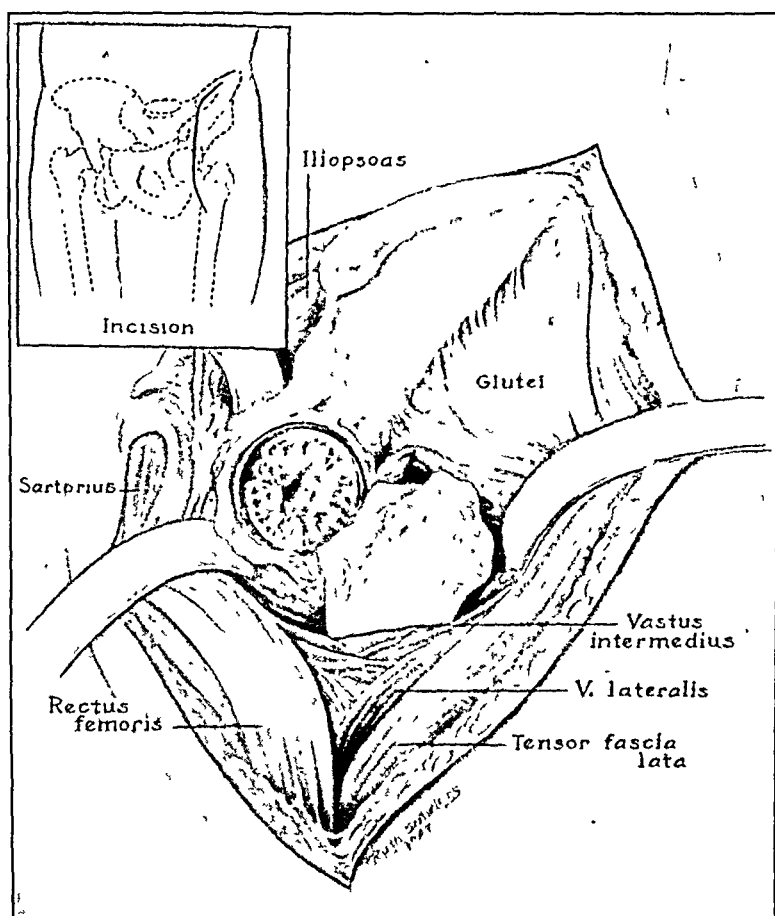


Fig. 1.—Exposure.

trochanter and a corresponding wedge fashioned from the superior rim of the acetabulum (fig. 2). The notch should not be over  $\frac{3}{8}$  inch (0.95 cm.) deep or the extremity will be unnecessarily shortened. It is often advantageous to cut off the lesser trochanter flush with the shaft so that it will not impinge on the posterior-inferior rim of the acetabulum. The greater trochanter is then placed in the acetabulum (fig. 3) and a Lorenzo screw<sup>2</sup> inserted under direct vision, aiming

2. Lorenzo, F. A.: Molybdenum Steel Lag Screw in Internal Fixation of Fractured Neck of Femur, *Surg., Gynec. & Obst.* **73**:99-104 (July) 1944.

somewhat superiorly and posteriorly into the thickest, firmest portion of the ilium. In most cases a  $3\frac{1}{2}$  or  $3\frac{3}{4}$  inch (8.8 or 9.5 cm.) Lorenzo screw will be long enough. If there is difficulty in retracting the tensor fasciae latae muscle far enough laterally to get the screw started, it may be cut transversely for a few centimeters. No secondary incision need be made. Good stability is present when the screw is tightened down. The position of fixation is 15 to 20 degrees flexion, 5 to 10 degrees abduction and slight external rotation. Flaps of bone are raised from the side of the ilium and upper end of the trochanter and strips of cancellous bone taken from the wing of the ilium and placed

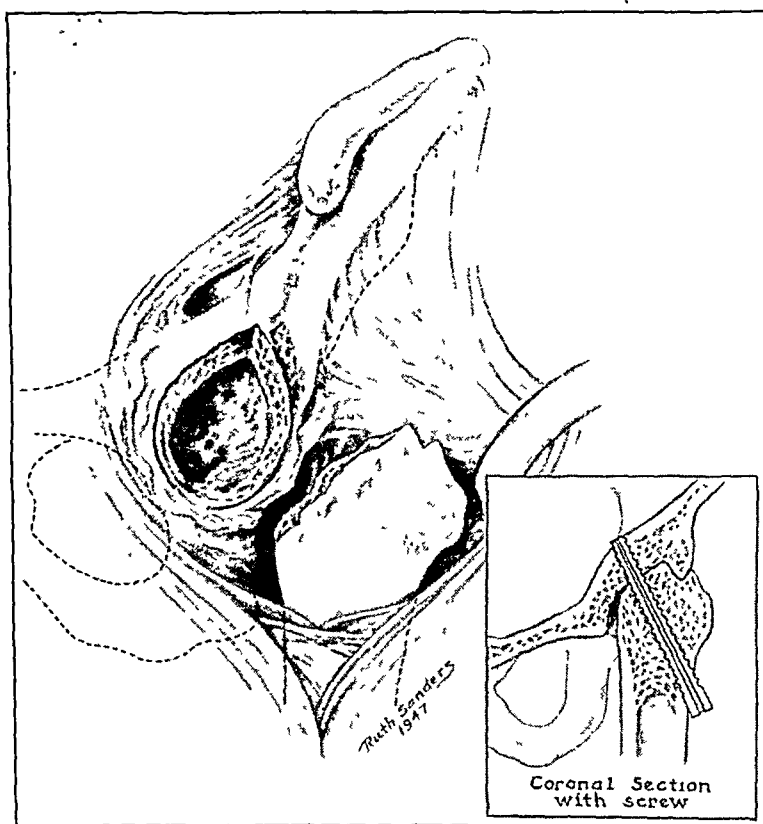


Fig. 2.—Note that the femur is placed directly under the acetabulum. Thus a constant impacting force is in effect.

under the flaps (fig. 3). If there is space between the femur and the deepest part of the acetabulum, this is packed with pure cancellous bone. Cortical bone is not used in this deep area because if postoperative infection should occur, removal of sequestrums would be extremely difficult. Cancellous bone does not form sequestrums readily.

The wound is closed in layers. The rectus and sartorius muscles are not reattached to bone. Since bone has already been removed from the iliac crest and the anterior-superior spine, closure is easy. A one and one-half spica is applied.

## POSTOPERATIVE TREATMENT

The spica is kept on until there is definite roentgenologic evidence of union. This will be three to three and a half months. A high single spica with a walking block is then applied and the patient allowed up on crutches until union is secure. Treatment without a cast was considered but not deemed advisable, for although the bone of the ilium is firm and strong that of the upper end of the femur is rather soft, and it

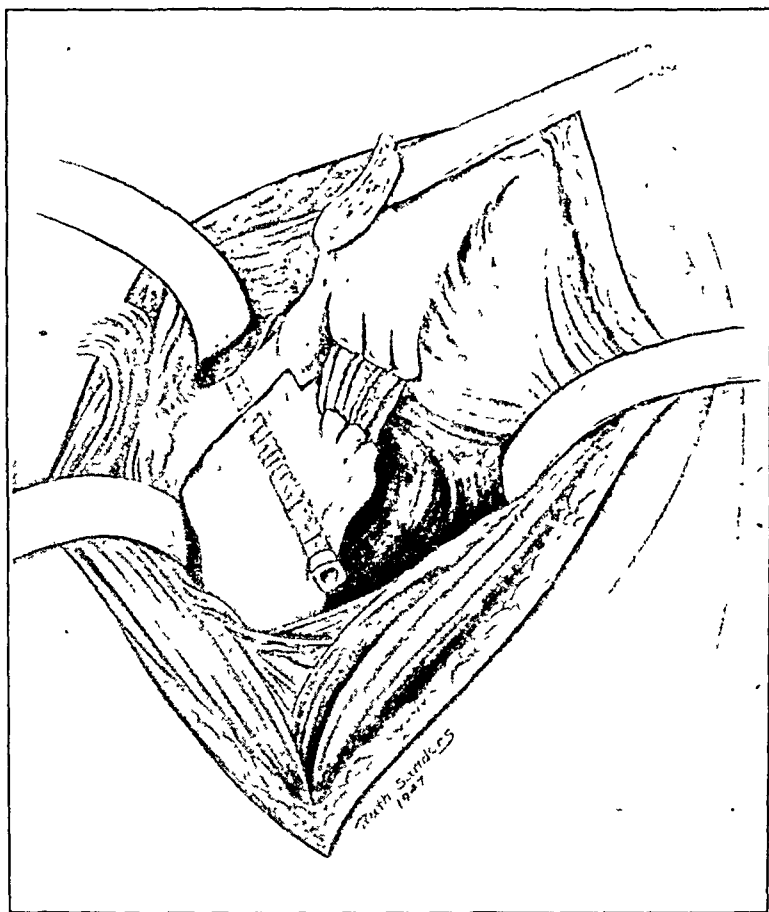


Fig. 3.—Operation completed except for closure.

is doubtful if a screw or a flanged nail alone would maintain the optimum position.

## COMMENT

We have used this technic in 7 cases, and enough time has elapsed so that the results can be surveyed. In the first cases a Smith-Petersen nail<sup>1</sup> (fig. 4) was used instead of a Lorenzo screw. It was found that the nail had a tendency to pull out and that even slight motion of the extremity might cause contact to be lost between the femur and the ilium. A Lorenzo screw was then tried and was found to work much

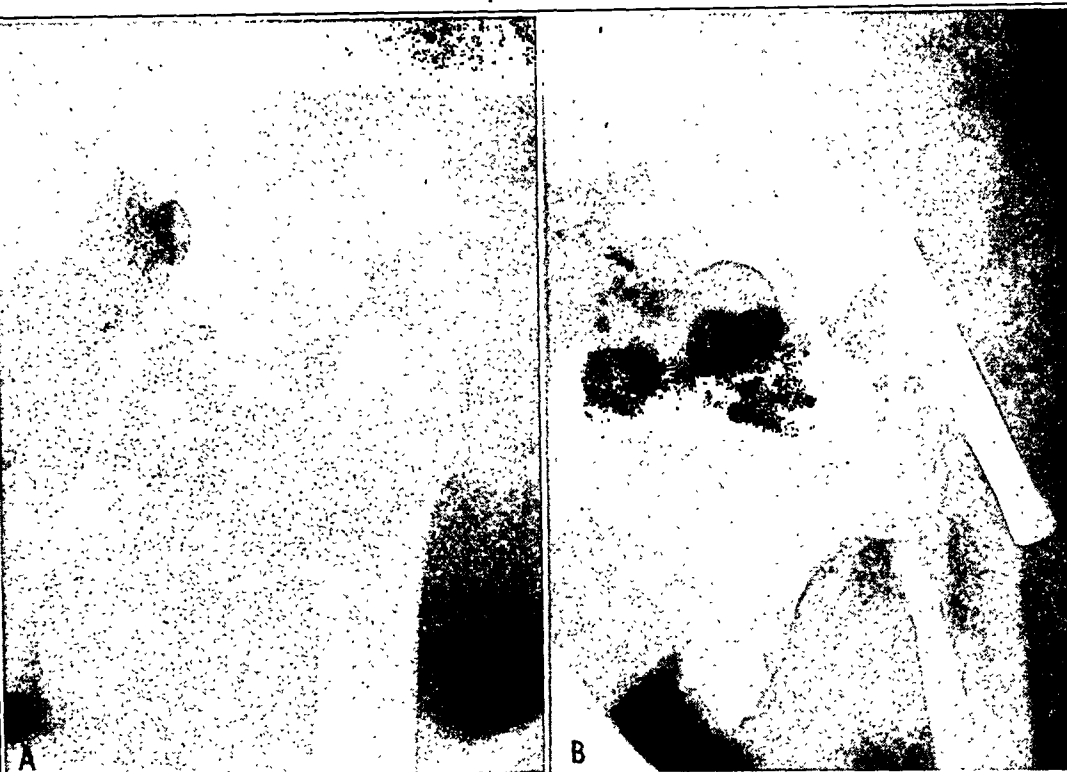


Fig. 4.—*A*, before operation. *B*, six months after arthrodesis using flanged nail.

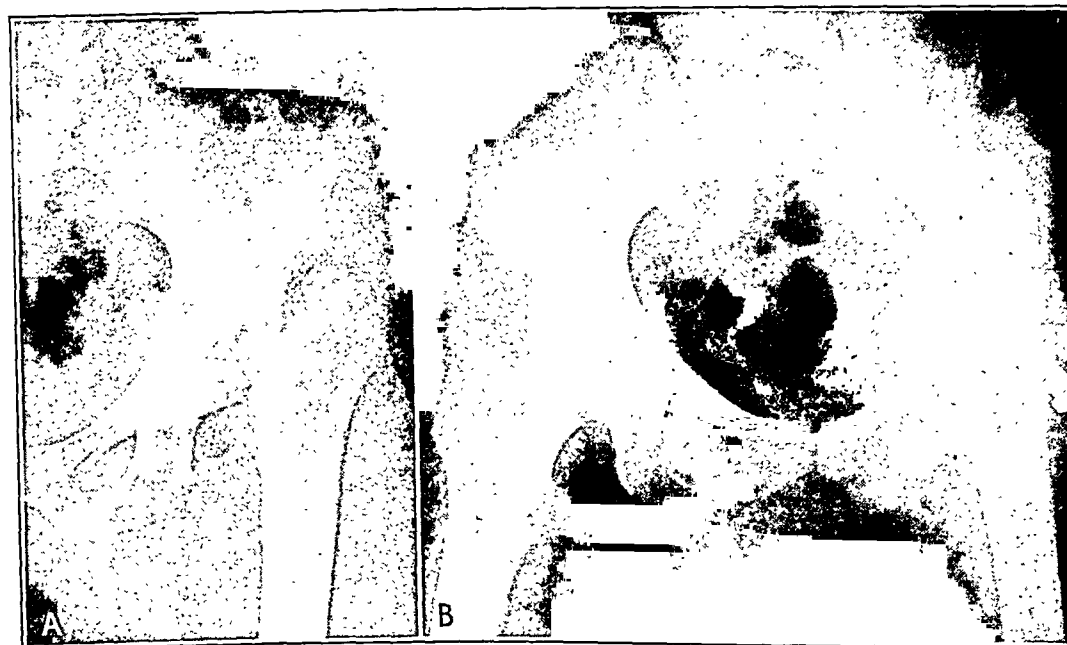


Fig. 5.—*A*, before operation. *B*, six months after arthrodesis using a Lorenzo screw.

better (figs. 5 and 6). Because of the deep threads a secure hold is obtained in the ilium and the bony surfaces can be pressed firmly together. Of the 7 operations done, 6 were successful. Fusion was solid and the patient ready to begin full weight bearing in an average of six months. The first operation performed by this technic represents the only failure. In retrospect the reasons are obvious. The scar tissue was not completely removed from the inferior portion of the acetabulum,

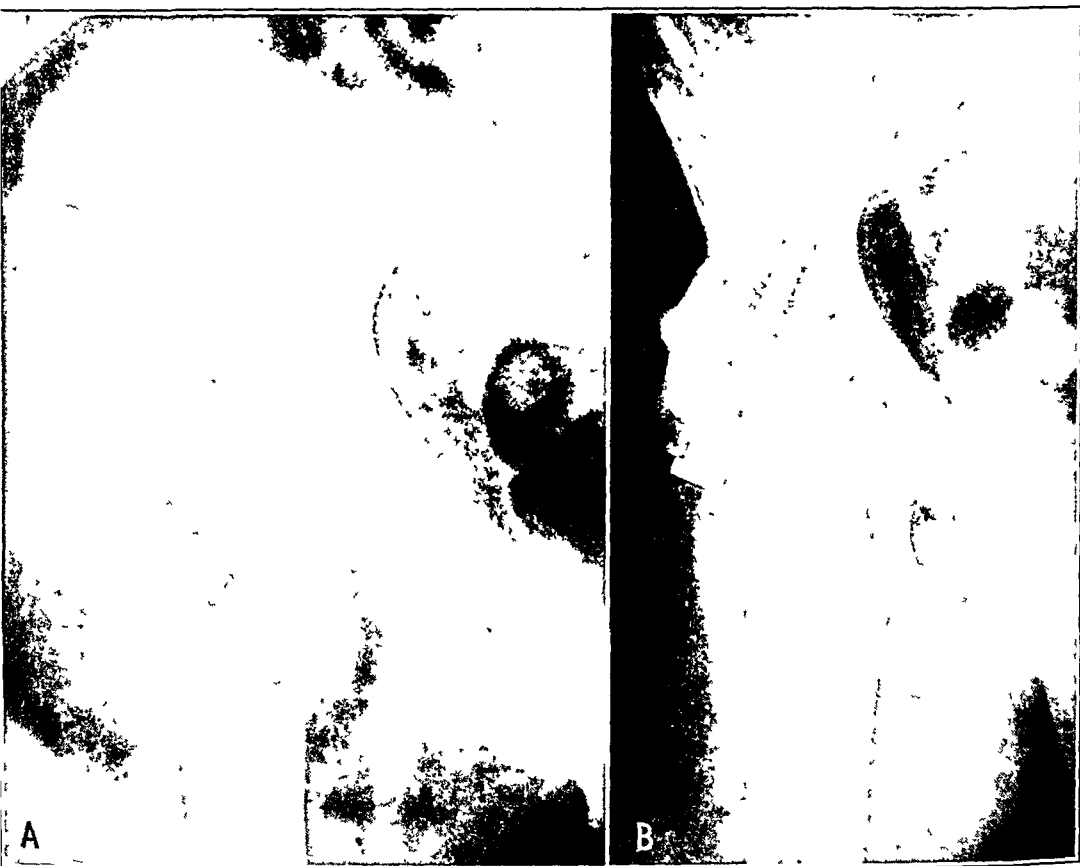


Fig. 6.—*A*, this patient first had a fractured neck of the femur. A flanged nail was inserted, but nonunion resulted. A high abduction osteotomy was done. Fusion occurred between the trochanter and the shaft, but the head remained loose and the hip unstable. Another reconstruction was tried, but infection occurred. The femoral head was removed because it had become a sequestrum. Arthrodesis was performed on March 27, 1947. *B*, roentgenogram taken on Oct. 1, 1947, approximately six months after operation.

and the femur could not be displaced far enough medially. Also, contact was lost because of pulling out of the flanged nail.

In 2 cases purulent drainage occurred postoperatively. Both patients had been heavily infected previously. One had been free of drainage for six months and the other for fifteen months. In the first case drainage stopped spontaneously after four weeks and the area remained dry.

Fusion was solid in the usual time. In the second case draining continued until the metallic internal fixation was removed three months postoperatively, and then it stopped and satisfactory fusion occurred.

Stripping the iliacus muscle from the inner surface of the wing of the ilium makes it possible to insert the screw in exactly the right place under direct vision, with no danger of penetrating too far into the pelvis. It also facilitates the notching of the anterior rim of the acetabulum. Since a cast is applied, this stripping adds little to postoperative morbidity.

There is about 1 to 1½ inches (2.5 to 3.8 cm.) of actual shortening of the extremity due to loss of bone substance. The flexion in which the hip is fused increases the shortening slightly, but some apparent length can be gained by abduction.

We prefer arthrodesis with the extremity in the longitudinal line of the body if there has been little loss of length, but when there is as much as ¾ inch (1.9 cm.) of shortening, some abduction is desirable.<sup>3</sup> However, we believe that the abduction should not exceed 10 degrees or undue strain will be put on the lumbar region of the spine and the knee.

Although the present series is not large, bony union has been obtained in a high percentage when it is considered that failure of fusion in this condition of the hip is notoriously frequent. By the technic described it is possible at operation to place the extremity in exactly the desired position in relation to the pelvis and hold it there until fusion is complete.

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3. The width of the pelvis affects the amount of apparent length that can be gained by abduction (Sedden, H. J.: *The Angle of Abduction of the Hip After Subtrochanteric Osteotomy*, *Lancet* **2**:552-555 [Sept. 3] 1938). The pelves of 14 cadavers (9 males and 5 females) were measured. The distance between the centers of rotation of the femoral heads ranged from 15.1 cm. to 18 cm., and the average was found to be 16.5 cm. With the use of this distance, calculations were made with an abduction osteotometer similar to the one described by Milch (Milch, H.: *Abduction Osteotometer*, *J. Bone & Joint Surg.* **24**:359-366 [April] 1942), and the following figures were obtained:

Degrees of Abduction of Shorter Extremity	Gain in Apparent Length of Shorter Extremity
0	0.0 cm.
5	1.5 cm.
10	2.9 cm.
15	4.3 cm.
20	5.7 cm.

Since the variation in width of normal pelves is relatively small, these figures are applicable for practical purposes.

## RELIEF OF CHRONIC HYPERTENSION BY EXCISION OF PHEOCHROMOCYTOMA

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THE CLINICAL picture generally associated with pheochromocytoma is one of paroxysms of hypertension with normal blood pressure in the intervals between attacks. That chronic hypertension may be produced by pheochromocytoma is well understood.<sup>1</sup> However, I intend to emphasize the importance of considering such a lesion as a real possibility in all cases of hypertension, especially when the explanation of the symptoms and the hypertension is not completely satisfactory.

The outcome in the patient afflicted with a pheochromocytoma is invariably fatal if the tumor is not removed. The hypertensive crises in those with a history of paroxysms become more and more severe until death results from a violent crisis. The organic cardiovascular changes in the person with chronic hypertension due to pheochromocytoma may not cause death as soon as those which occur in the paroxysmal type, but the outcome is as inexorably fatal. Every precaution must be taken to diagnose the presence of such a tumor in cases of paroxysmal or chronic hypertension in order that a cure may be effected. A diagnosis of diabetes or hyperthyroidism is often made before the true nature of the disease is revealed.

The history may not suggest the presence of paroxysmal attacks, particularly in cases of chronic hypertension. The diagnosis and localization of the tumor is difficult. Both adrenal regions should be explored routinely at the time of sympathectomy for hypertension. However, the tumor may not lie in the adrenal regions but may arise wherever chromaffin tissue is found.

Tests for this epinephrine-producing tumor have been devised to assist in the diagnosis. The first test is the histamine test,<sup>2</sup> in which 0.05 mg. of histamine in 0.5 cc. of isotonic sodium chloride solution or 0.025 mg. in 0.25 cc. of solution is injected intravenously and the

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From the Department of Surgery of the University of Chicago.

1. Green, D. M.: Pheochromocytoma and Chronic Hypertension, *J. A. M. A.* **131**:1260-1265 (Aug. 17) 1946. Soffer, L.; Mencher, W. H., and Colp, R.: Pheochromocytoma of Adrenal Gland, *S. Clin. North America* **26**:368-381, 1946.

2. Roth, G. M., and Kvale, W. F.: A Tentative Test for Pheochromocytoma, *Am. J. M. Sc.* **210**:653-660, 1945.

blood pressure is determined every minute after injection. A marked rise of blood pressure (a 110 to 140 mm. rise in systolic pressure and a 30 to 75 mm. rise in diastolic pressure) is reported to follow the administration of histamine in the presence of epinephrine-producing tumors. Such responses are not obtained in patients with hypertensive vascular disease or in normal patients. This test was worked out by Roth and Kvale.

A second "new test" is based on the use of adrenolytic drugs. Goldenberg and his co-workers<sup>3</sup> have reported that benzodioxane causes lowering of the systolic and diastolic blood pressure of patients suffering from chronic hypertension as a result of pheochromocytoma. There is no lowering of systolic or diastolic pressure in cases of hypertensive vascular disease or of arteriosclerotic hypertension. Their experience with this drug in instances of pheochromocytoma and hypertensive vascular disease is such that it promises to be of great value in determining the presence of epinephrine-producing tumors.

Our interest in this subject has been stimulated by recent experience with a young woman suffering from hypertension who was seen at this hospital. Her history was one which might have been given by any person suffering from hypertensive vascular disease, and prior to the time she had been seen here she had been studied carefully and advised to undergo sympathectomy. During the process of study in the clinic for renovascular diseases the patient was admitted to the hospital because of suspected appendicitis. This disease was not present, but during the process of study a mass was felt in the midepigastrium. The discovery of this mass led to the diagnosis.

#### REPORT OF A CASE

The patient, a white woman 25 years of age, was admitted to Albert Merritt Billings Hospital on Feb. 19, 1947. Her complaints dated back to four years previously, at which time, during an examination for employment, she was told that she had a blood pressure of 150 systolic and 100 diastolic. Since that time she had noted shortness of breath on many occasions, not necessarily related to activity. She believed that she had episodes when she felt excited and nauseated; at the same time she had nervous and anxious feelings. During the past four years she had suffered from severe sweating over the entire body, becoming progressively worse in recent months. In the past year she had experienced dizzy spells accompanied with shortness of breath. These occurred in the morning on arising or at other times of the day, especially when standing, and they were relieved by sitting down. When the attacks occurred in the morning there was associated blueness of the legs.

During the nervous attacks she often had pain over the heart, with radiation. The pain was accompanied with shortness of breath, palpitation and skipped

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3. Goldenberg, M.; Snyder, C. H., and Aranow, H.: A New Test for Hypertension Due to Circulating Epinephrine, *J. A. M. A.* **135**:971-976 (Dec. 13) 1947.



beats. Fainting spells had been frequent in the past four months. She also complained that for six months she had experienced a constant "beltlike" pain in the upper part of the abdomen radiating through to the back.

In June of 1946 she underwent a complete study elsewhere. At that time intravenous pyelograms, a sodium amytal test and renal function tests were made. The patient was advised to undergo sympathectomy for the relief of the hypertension, but she declined this treatment. She was then treated with thiocyanates, papaverine and rutin in conjunction with a low salt diet and psychotherapy. At one time she was told she had diabetes. Systemic examination revealed nothing significant except for the factors noted previously. Her menstrual history revealed menarche at the age of 13, with regular periods occurring each twenty-eight days and lasting five days. The family history was significant in that her father had hypertension and died of carcinoma.

*Physical Examination.*—Physical examination revealed a well developed, tall, somewhat thin woman of the apparent age of 25 years. The hair was normal, and there were no bony abnormalities of the head. The pupils were round, regular and equal and reacted to light and in accommodation. The fields were normal. The eyes were prominent. The disks were normal. The arterioles were constricted, and the ratio of arterioles to veins was 1:3. No hemorrhages or exudates were present. The ears were normal on gross testing and examination. The nose and mouth were essentially normal. There were no masses in the neck.

The chest was symmetric. There were several areas of small, tender soft nodules on the both breasts. The lungs were clear to percussion and auscultation. Expansion was full and equal.

The heart was not enlarged. An occasional extrasystole was heard. A long blowing systolic murmur, loudest at the apex, was heard through the precordium. The blood pressure was 185 systolic and 125 diastolic.

Diffuse tenderness was present over the abdomen, more on the right side. A mass measuring 2 by 2 inches (5 by 5 cm.) was palpable in the left upper quadrant near the costal margin. It did not move with respiration. Slight enlargement of the right ovary was noted; otherwise the pelvic organs were normal. One large external hemorrhoidal tag was found in the rectum. The extremities were normal. The distribution of body hair was within normal limits.

*Laboratory Examination.*—Laboratory examinations at the time of admission gave the following results: The specific gravity of the urine was 1.023, and there was a slight trace of albumin. There was no sugar in the urine. Microscopic examination revealed an occasional red cell. The hemoglobin content of the blood was 13.6 Gm. per hundred cubic centimeters, the red blood cell count 4,690,000, and the white blood cell count 7,700. The Wassermann and Kahn tests gave negative results. The nonprotein nitrogen was 21, the urea nitrogen 7.8 and urea clearance 100 per cent of normal.

*Other Studies.*—Electrocardiographic studies revealed a small Q wave in leads II and III, a low T wave in lead I, an extremely low T wave in lead II and an inverted T wave in lead CF. The report was "myocardial abnormality, with slight tendency to right axis deviation; the axis is unusual for uncomplicated hypertension."

Roentgenograms of the chest, kidneys, stomach, duodenum and colon were normal.

On Feb. 23, 1947, a test with amobarbital sodium (amytal sodium®) revealed an initial blood pressure of 198 systolic and 124 diastolic. The lowest reading was

recorded at six hours; this was 140 systolic and 90 diastolic. At twelve hours the pressure had risen to 170 systolic and 130 diastolic. On February 24 a histamine test<sup>2</sup> gave no response which could be interpreted as indicative of the presence of pheochromocytoma. This should have been repeated with a stronger dose of histamine. The benzodioxane test<sup>3</sup> was not done.

Because of the palpable abdominal tumor with hypertension and a history of attacks which were suggestive of paroxysmal hypertension, it was felt that intra-abdominal exploration was indicated. None of the attacks had been witnessed by any of the attending physicians or nurses.

Operation was undertaken on March 15 under continuous spinal, ethylene and oxygen anesthesia.

*Operation.*—The abdomen was opened through an upper midline incision. A tumor mass, which was round and firm, was palpated just to the left of the lumbar

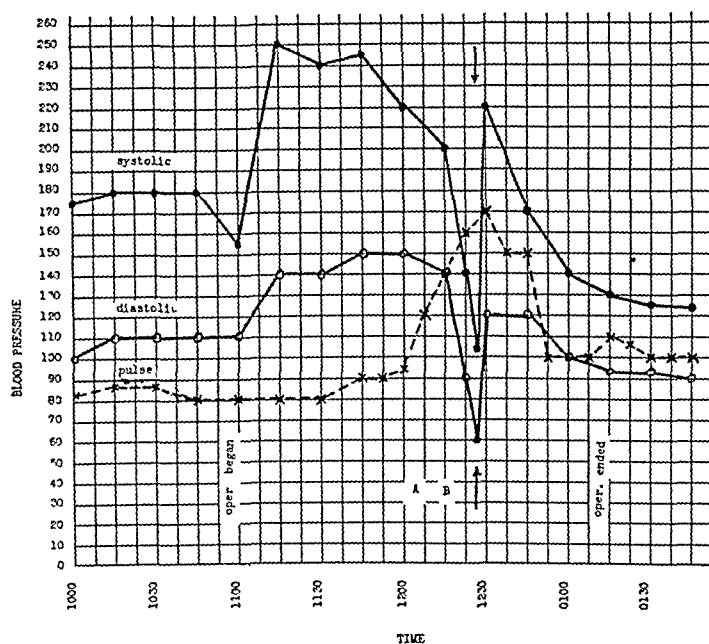


Fig. 1.—Blood pressure readings during operation. Manipulation of the tumor began at A. Pedicle of the tumor was clamped at B. At the point marked by the arrow the patient received 0.024 Gm. of ephedrine intravenously.

region of the spine at the level of the third lumbar vertebra. Exploration of the right upper part of the abdomen revealed no abnormalities. Both adrenals were explored and were found to be normal. Three small cysts were present in the right ovary.

The tumor mass on the left side of the abdomen was exposed by retracting the jejunum medially. It was then found that it lay in the retroperitoneal tissues directly over the left lumbar sympathetic chain just medial to the ligament of Treitz and against the left side of the aorta. The mass was approximately 6 cm. in diameter, had a firm capsule and was well demarcated from the surrounding tissues. It was copiously supplied with blood vessels on all sides, but the main vessels came from the posterior aspect of the tumor. It was pink and resilient.

The peritoneum was incised over the tumor, and the latter was dissected free from the surrounding tissues, a small amount of areolar tissue being left on its surface. Numerous nerve fibers were found to run into the posterior aspect of the tumor mass from the left lumbar sympathetic chain. During the manipulation of the tumor the blood pressure and pulse rate had steadily increased, so that just before the last vessels were clamped the blood pressure was 220 systolic and 160 diastolic and the pulse rate 160 (fig. 1).

As the main pedicle was clamped the blood pressure fell precipitously to 100 and the pulse rate began to decline. When the pressure reached 100 ephedrine was given intravenously in an attempt to forestall further fall. Response to the ephedrine was prompt, and the pressure finally stabilized at 120 systolic and 96 diastolic and the pulse rate at 100. The postoperative course was uneventful.

The preoperative and postoperative blood pressure readings are graphically represented in figure 2.

The patient was discharged from the hospital in excellent condition twelve days postoperatively. She was followed as an outpatient. One month after her

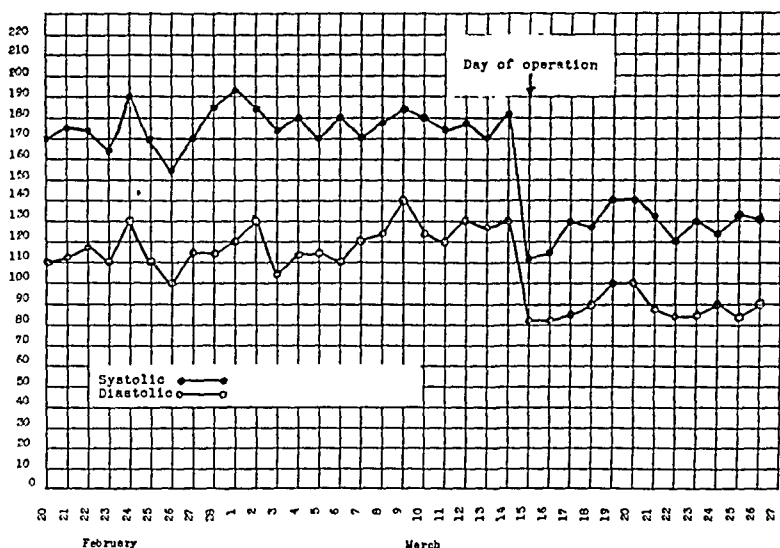


Fig. 2.—Daily average blood pressure readings over a thirty-five day period.

discharge she complained of feeling cold when others about her were hot. Otherwise she felt in good condition. Her basal metabolic rate was +4 and the blood pressure 124 systolic and 94 diastolic.

In September she continued to complain of feeling cold. Her blood pressure was 126 systolic and 94 diastolic. Her general condition was satisfactory. Up to the present time the blood pressure has remained in the vicinity of 124 systolic and 94 diastolic.

**Pathologic Report.**—Gross Examination: The specimen consisted of a smooth, oval, encapsulated tumor, weighing 65 Gm. and measuring 5 by 4 by 4 cm. The surface was pink and finely fibrous and exhibited adherent tags of ligated blood vessels. The cut surfaces bulged and were soft but elastic and grayish pink. They contained many small pockets containing bloody fluid. When a piece of tumor tissue was placed in 3 per cent potassium dichromate, it quickly turned brown (5 to 10 minutes). After 20 minutes the tumor tissue was brown-black, while the capsule was pale yellow (positive chromaffin reaction).

*Microscopic Examination.*—This was a vascular cellular tumor, with the cells arranged in trabeculae and nests of widely varying sizes, separated from vascular spaces (fig. 3). Some of these were thin-walled sinuses, others were like venules and others were thin-walled large veins, often surrounded by fibrous tissue. The abundance of the small sinuses was well shown by the Mallory connective tissue stain. The cells were pleomorphic. In some regions they closely resembled normal medullary cells of the adrenal gland. Other cells were large, round or stellate. The cytoplasm of most of the cells was granular, but in some cells there were vacuoles.

In frozen sections the only cells containing coarse sudanophilic globules or granules lay in or near the walls of blood sinuses and appeared to be histiocytes or endothelial cells.

Of special value were slides prepared from the chromated fresh tissue. Four fifths or more of the cells had deep brown cytoplasm, appearing finely granular

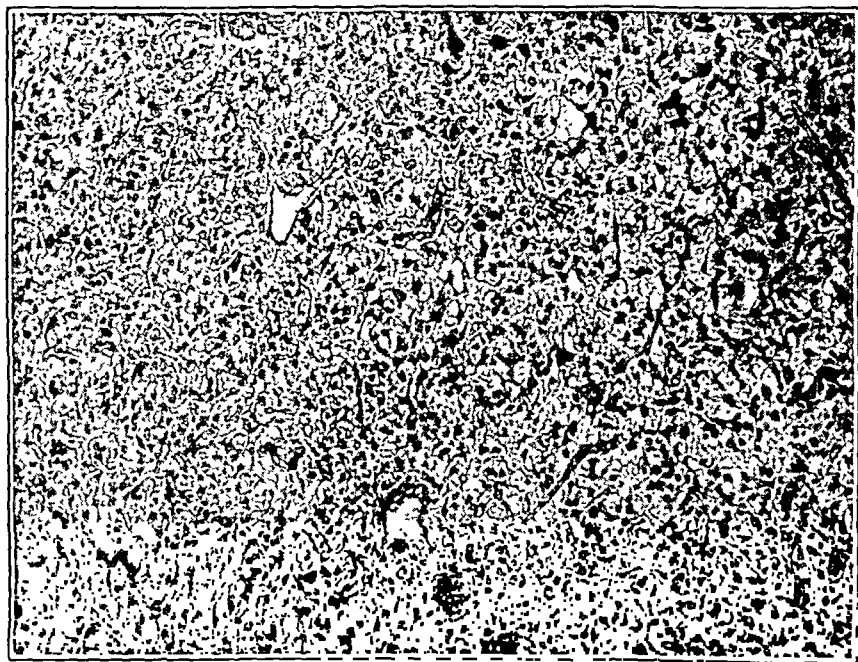


Fig. 3.—Microscopic section of the tumor.

under high power magnification. Since only an occasional brown granule (iron or lipochrome) was seen in the formaldehyde-fixed sections, the chromatin must be attributed to the presence of precursors of epinephrine. The cells which were the least chromated were, in general, the large cells with large dark nuclei. No extremely small (primitive) cells or ganglion cells were included within the tumor. However, the fibrous capsule contained nerve trunks, and strung along the nerves were scattered ganglion cells. The sections fixed in Zenker's solution were slightly chromated but much less uniformly than the sections fixed in dichromate followed by dichromate-formaldehyde.

The impression gained was of a characteristic benign pheochromocytoma or chromaffin tumor of sympathetic neural origin arising in the abnormal sympathetic chain, in the vicinity of the Zuckerkandl organ. From the intense chromaffinity, one would expect a high content of epinephrine.

Biochemical assay of the tumor by the Folin method revealed an epinephrine content of 25 mg. per gram of tissue. This represents a total of 1,625 mg. of epinephrine contained in the tumor. By comparison with the epinephrine content of previously reported tumors this represents a high concentration.

The normal adrenal gland contains 1 to 2 mg. of epinephrine per gram of tissue. Other authors have reported assays of tumors revealing anywhere from 1 mg. to 30 mg. of epinephrine per gram.<sup>4</sup> However, the majority of the reports record concentrations of less than 10 mg. per gram.

Why one tumor should cause paroxysmal hypertension and another cause chronic hypertension is difficult to explain. Beer, King and Prinzmetal<sup>5</sup> and also Hyman and Mencher<sup>6</sup> reported demonstrating the presence of a pressor substance in the blood of a patient during a paroxysm. Possibly there is a continuous secretion of epinephrine by the tumor in some persons, but intermittent secretion in others. In dogs it is impossible to create permanent hypertension by continuous infusion of epinephrine for two weeks.<sup>7</sup> Instead of producing hypertension the dose required becomes toxic and kills the dog. Of course the condition is not as chronic in such an experiment as it is in the case of the person with an epinephrine-producing tumor. It is attractive to surmise that the paroxysms result from sudden release of epinephrine from the tumor mediated by the same mechanism as the release of epinephrine from the adrenal glands. Whether or not there may be excess cortical hormone secretion in cases in which there is chronic hypertension is unknown. No cortical tissue was found in sections of this tumor.

It is interesting that prior to removal of the tumor this patient was troubled by excessive perspiration and was always hot but after the removal of the tumor she did not perspire and constantly felt cold. Unfortunately her basal metabolic rate was not determined prior to operation, but two months postoperatively it was +4. The secretion of epinephrine causes a rise in basal metabolic rate not mediated by the thyroid. It is common to find considerable elevation of the basal metabolic rate in patients with this tumor, and it is possible that during her four years of hypertension the patient had become accustomed to an increased basal rate, so that after its return to normal she felt cold when others were warm.

#### SUMMARY

A case of chronic hypertension caused by pheochromocytoma and cured by the removal of the tumor is herein reported.

The extra-adrenal location of the tumor emphasizes the fact that exploration of the adrenals at the time of sympathectomy may not reveal the tumor.

Tests for epinephrine-producing tumors are simple and can be utilized to advantage in the study of the hypertensive patient.

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4. Brunschwig, A.; Humphreys, E., and Roome, N.: The Relief of Paroxysmal Hypertension by Excision of Pheochromocytoma, *Surgery* 4:361-370, 1938.

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## DRILL PERFORATION, A SIMPLIFIED METHOD FOR VENTRICULAR PUNCTURE

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AND

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**D**RILL perforation of the cranium to our knowledge has not been employed in recent years except by a few neurologic surgeons.<sup>1</sup> The simplicity of the method and the rapidity with which it can be carried out make it especially suitable for the emergency treatment of the patient with increased intracranial pressure. At first glance it may be considered hazardous because of possible hemorrhage from ruptured cortical vessels. Our experience, however, indicates that it is safe when performed on patients with increased intracranial pressure and with due regard to anatomic and physiologic factors.

### METHOD

Perforation of the skull is performed by the use of a simple twist drill point 2 mm. in diameter (fig. 1). The dura mater can be perforated in a like fashion or by the use of an 18 gage lumbar puncture needle. Since the ventricular needle has little or no leeway in this small opening, it is important that the drill opening in the skull be accurately placed with due regard for the direction to the ventricle which it is desired to puncture.

After the appropriate area of the scalp is shaved and the head positioned, the support under the patient's head is draped with sterile towels and the scalp is sterilized in the usual fashion. The midline is identified by palpation of the external occipital protuberance while the assistant places his extended index finger on the nasion. The sites of the projected drill holes, whether frontal or occipital, are marked with iodine-moistened applicators. For the occipital approach we use a point 6 cm. anterior to the inion and 5 cm. lateral to the midline. These areas are infiltrated with 0.5 per cent procaine hydrochloride solution

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1. Dr. W. V. Cone has brought the procedure to a high state of perfection. When we first began to use this method, we received several valuable suggestions from observation of his technic.

containing 5 drops of epinephrine solution (1:1,000) in 100 cc., and care is taken to inject it beneath the periosteum. With the use of a sharp-pointed scalpel such as the Bard Parker no. 11, stab wounds approximately 3 to 4 mm. in length are made in the scalp. The blunt end of the no. 7 Bard Parker knife handle is inserted into the wound as a periosteal elevator and separates the pericranium from the skull. Manual pressure is applied to the stab wound with sterile gauze sponges, and the assistant applies counter pressure with his hand on the frontal region. Hemostasis is usually gained within one minute. Only rarely must a silk suture be inserted for hemostasis. The small drill (2 mm. in

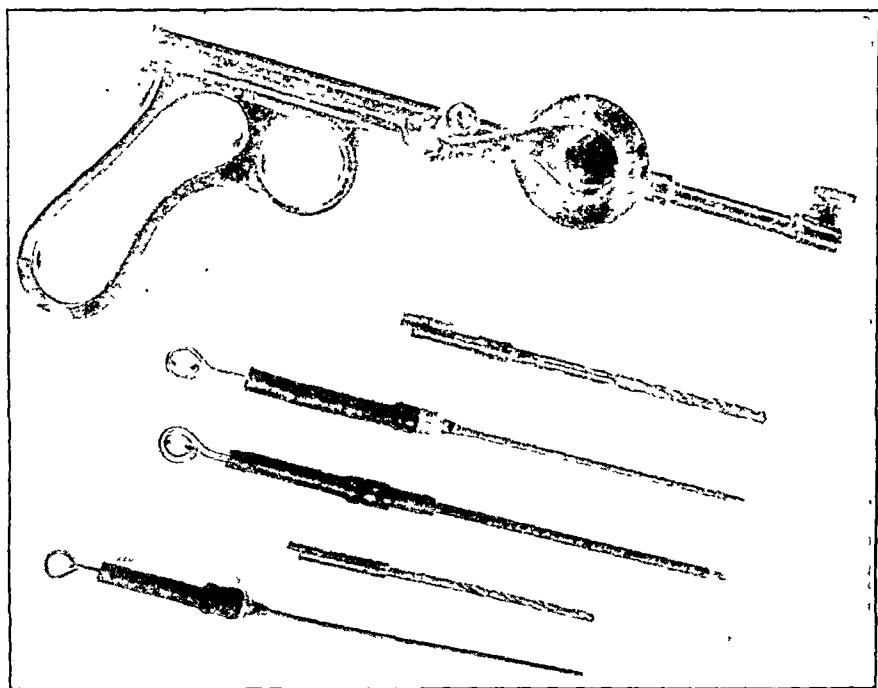


Fig. 1.—Drill handle, twist drill points and ventricular needle used in procedures.

diameter) is customarily used and is carefully directed toward the nasion (fig. 2). During insertion of the drill point, distortion of the scalp is prevented, for this causes difficulty in finding the small drill hole when the ventricular puncture is attempted. Accuracy of the drill direction is maintained, since the narrow size of the drill hole provides little leeway in subsequently altering the direction of the needle.

The drilling is performed with dispatch. The varying resistances of the outer table, the diploic space and the inner table of the skull being distinguished, the dura mater is pierced quickly. Dural penetration may be accompanied with momentary pain, and the operator hears a distinct "pop." The dura mater is penetrated with the drill turning rapidly, for

it is felt that the circular motion of the drill helps seal the encountered vessels. Sudden rapid penetration of the dura with the drill is of utmost importance in avoiding any possibility of extradural hemorrhage. As the drill is removed, there may be a slight gush of blood and cerebrospinal fluid, which usually subsides in less than twenty seconds. Local pressure over the stab wound is avoided at this stage because it is desirable that any slight dural or cortical bleeding be drained externally. If necessary, pressure may be applied below the stab wound over the occipital arteries to control any bleeding from the scalp.

The small ventricular needle is inserted slowly through the drill hole into the brain. The ventricle is usually encountered at a depth of

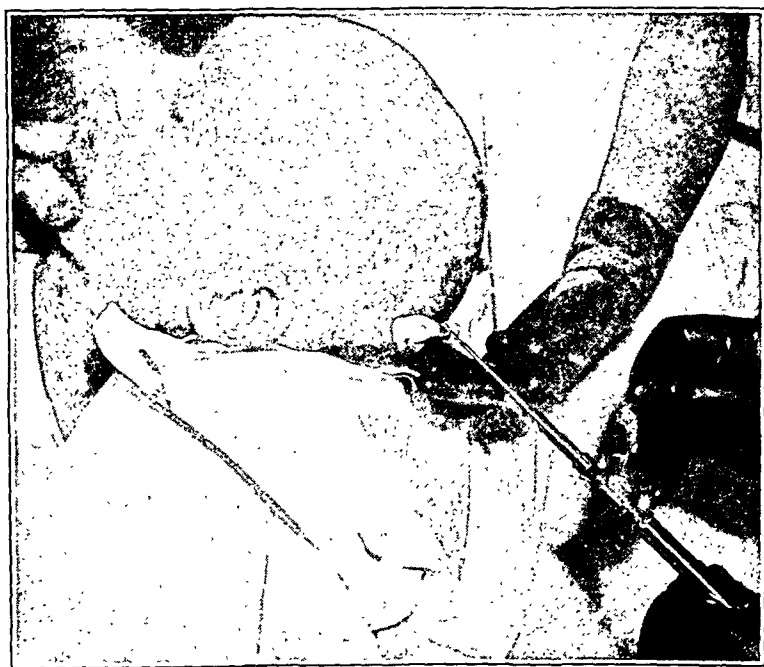


Fig. 2.—Technic of drill perforation.

5 to 7 cm. Replacement of the ventricular fluid with filtered air or oxygen is then carried out, or if simple ventricular drainage is desired the fluid is allowed to flow out freely.

One advantage of this method is particularly apparent at this stage in that there is less danger of the needle shifting because it is more rigidly held in place by the scalp and skull than in ventricular puncture through ordinary trephine openings.

Because of the simplicity of this method and the rapidity with which ventricular puncture can be carried out, it is especially useful as an emergency procedure. For this purpose we keep available at all times a sterile wrapped tray containing ventricular needles, 2 and 4 mm. drill



points and drill handles as well as the usual syringes, hypodermic needles and sponges.

#### COMMENT

The drill perforation technic may be regarded as a revival of the brain puncture or ventricle puncture methods practiced more extensively in the early part of the century. Reference to the early literature as well as the discussion of the earlier technic is contained in the book by Krause.<sup>2</sup> Later reference to similar methods is found in an article by Purves-Stewart.<sup>3</sup> No doubt this method fell into disrepute through being employed without due consideration for more definitive treat-

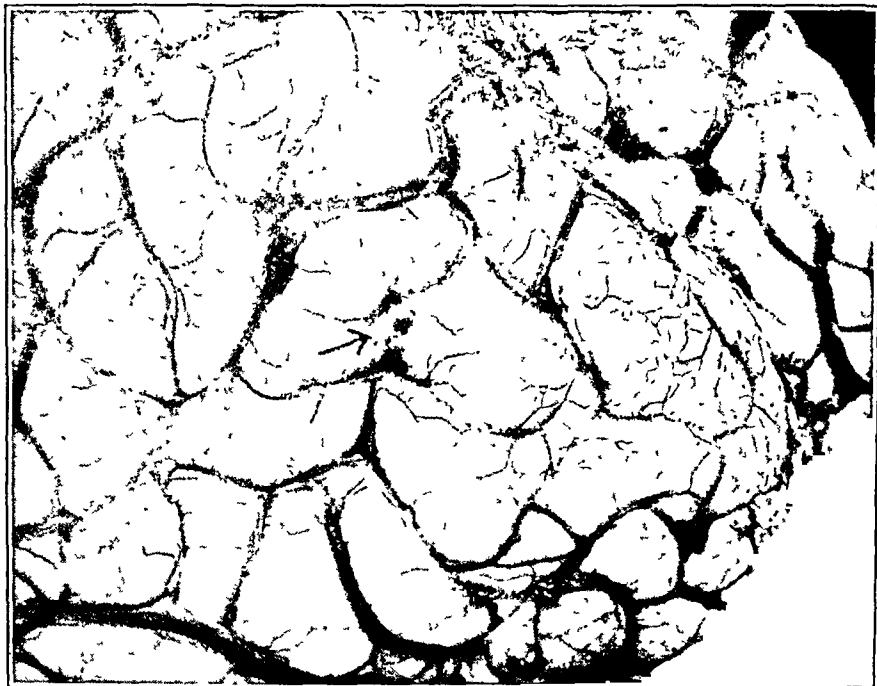


Fig. 3.—Cerebral cortex (left occipital lobe) of patient who died from glioblastoma multiforme seven days after operation, which was preceded by drill ventriculography. The site of puncture is indicated by the arrow.

ment. As a blind procedure it has inherent limitations and dangers which must be taken into consideration. However, our experience indicates that it is no more likely to be attended by complication than is ventricular puncture through an open burr hole.

In reviewing the first hundred cases in which we performed drill perforation with subsequent ventricular puncture, ventriculography or

2. Krause, F.: *Surgery of the Brain and Spinal Cord*, translated by H. A. Haubold, London, H. K. Lewis, 1910, vol. 1.

3. Purves-Stewart, J.: Triple Puncture of the Brain, Cistern, and Ventricle, *Lancet* 2:1159-1162, 1925.

cerebral biopsy, we found no case in which a fatality could be ascribed to this procedure. Inspection of the dura and the cortex has been made at subsequent craniotomy and at autopsy. Most of them have shown no visible hemorrhage whatsoever (figs. 3 and 4), the 1 or 2 mm. opening in the dura and the cortex being barely visible to the naked eye. In a few instances there have been small areas, 1 to 3 cm. in diameter, of subdural or subarachnoid hemorrhage. These have never been more than a fraction of a millimeter in thickness, no more than may be seen surrounding punctures done through burr holes made in the course of the more conventional ventriculographic procedures. Extradural, subdural or intracerebral hemorrhage has been occasionally reported with



Fig. 4.—Coronal section of brain shown in figure 3. The needle tract is indicated by the arrow.

the more conventional methods of ventricular puncture. It is theoretically possible that the drill penetration may also cause serious hemorrhage from dural or cortical vessels, but experience indicates that it is unlikely if the site of the procedure is chosen with due regard for the location of the dural and cerebral vessels. The rapidly turning twist drill may be a factor in promoting quick sealing of blood vessels which may by chance be encountered. Sudden penetration of the dura is important in avoiding extradural bleeding. By avoidance of local pressure directly over the drill hole immediately after perforation of the cranium and the dura, bleeding which may occur will be drained extracranially until spontaneous hemostasis can take place. The procedure should no doubt be limited to patients with increased intracranial pressure, for

the higher pressure seals the subdural and subarachnoid spaces sufficiently to prevent appreciable hemorrhage.

The advantages of the drill perforation technic are several. First is its comparative simplicity and the saving of time for the patient and the surgical and nursing staffs. An operating room set-up is not required, and it may be done in the radiology department or at the bedside in an emergency in five or ten minutes. The second advantage is in the reduction of the size of the wound to a small stab wound so that removal of sutures is eliminated and dressings are reduced to a minimum. In the case of suspected glioblastoma multiforme, material for a biopsy may often be obtained through a drill perforation, which confirms the diagnosis and possibly eliminates the necessity of an exploratory craniotomy.

Several subdural hematomas have been diagnosed by this method by the gush of dark old blood when the dura was penetrated. However, in a case of suspected subdural hematoma trephination is without doubt preferable to this technic.

#### SUMMARY AND CONCLUSIONS

Experience with the technic of drill perforation over a period of four years indicates that it is a valuable adjunct to the armamentarium of the neurologic surgeon in the performance of ventricular puncture and cerebral biopsy. The simplicity of the procedure and the saving of time for the patient recommend it as an emergency procedure. No serious complications have been encountered in over 100 patients, and it may be considered to be relatively safe when carried out with due precaution by a properly trained surgeon. The important details in technic are described, and it is emphasized that it should be employed only in patients with evidence of increased intracranial pressure.

# XANTHOMATOUS GIANT CELL TUMORS ARISING IN SOFT TISSUE

Report of An Instance of Malignant Growth

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AND

SAMUEL PERLOW, M.D.

CHICAGO

THERE has been considerable controversy about the malignant nature of xanthomatous giant cell tumors arising in soft tissues. Of the lesions noted in tendons and tendon sheaths Fleissig<sup>1</sup> stated that there is no authentic record of metastatic growth. A similar conclusion has likewise been reached by Gomori<sup>2</sup> and Bussebaum<sup>3</sup> and by Berger<sup>4</sup> in a more general appraisal of the problem.

There have been, however, various indications that tumors of this nature may be malignant. Berger<sup>4</sup> cited an example in which local invasive qualities were noted in a growth originating in the thigh. Tourneux<sup>5</sup> reported an instance recorded by Gaudiani wherein a giant cell tumor metastasized to the regional lymph nodes. Similarly, he cited a case described by Dor, who treated a tumor on the index finger diagnosed as sarcoma myeloplaxes. This mass was excised, but it recurred locally and apparently then spread generally. Histologic features simulating those of a malignant process have been reported in specimens observed by King<sup>6</sup> and by De Santo, Tennant and Rosahn<sup>7</sup>.

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From the Department of Surgery, Michael Reese Hospital.

1. Fleissig, J., cited by Bussebaum.<sup>3</sup>

2. Gomori, G.: Three Uncommon Tumors, *Am. J. Surg.* **33**:150-156 (July) 1936.

3. Bussebaum, G.: A Contribution on Inflammatory Tumors Presenting the Picture of Malignant Tumors with a Consideration of So-Called Giant Cell Sarcoma of the Tendon Sheaths, Dissertation, Halle-Wittenberg, 1935; abstracted, *Internat. Abstr. Surg.* **62**:368 (April) 1936.

4. Berger, L.: Synovial Sarcomas in Serous Bursae and Tendon Sheaths, *Am. J. Cancer* **34**:501-539 (Dec.) 1938.

5. Tourneux, J. P.: Les sarcomes des gaines tendineuses, *Rev. de chir.* **47**:817-854, 1913.

6. King, E. S. J.: Concerning the Pathology of Tumors of Tendon Sheaths, *Brit. J. Surg.* **18**:594-617 (April) 1931.

7. De Santo, D. A.; Tennant, R., and Rosahn, P. D.: Synovial Sarcomas in Joints, Bursae and Tendon Sheaths, *Surg., Gynec. & Obst.* **72**:951-981 (June) 1941.

## REPORT OF A CASE

The patient, a 60 year old white man, was first seen in the Mandel Clinic of Michael Reese Hospital on March 18, 1946, complaining of a "lump" on his arm. This had been observed for five months and apparently had evolved slowly without pain. Examination revealed a round mass approximately 3 cm. in diameter on the lateral surface of the arm, just above the elbow. On palpation it was cystic though freely movable. It seemed to be attached slightly to the skin and was neither tender nor inflamed. However, a week later it became infected. The impression at the time was that the lesion was an infected sebaceous cyst, though the possibility of a neurofibroma was not excluded.

By April 4, 1946, the infection had subsided and the mass was easily shelled out. On July 16 a local recurrence of the tumor was noted, and the patient was hospitalized on August 13. Axillary nodes were not palpable. A roentgeno-

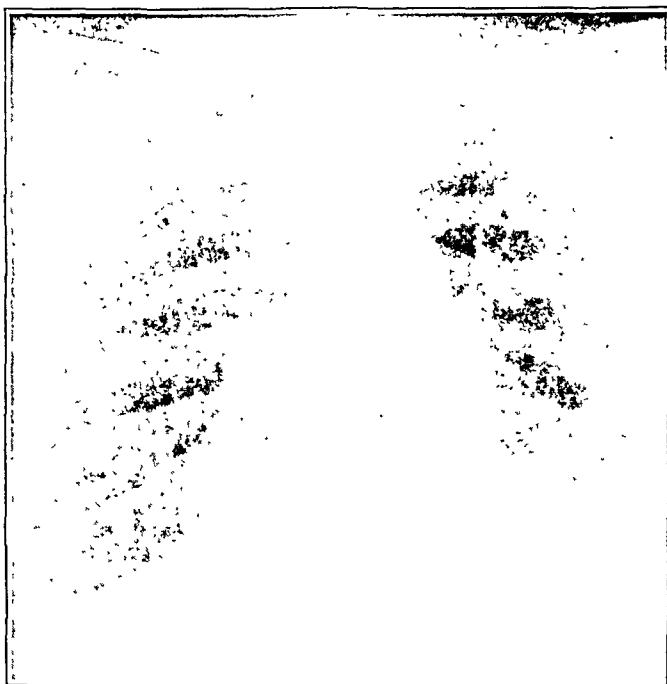


Fig. 1.—Roentgenogram of the chest at time of fourth local recurrence of tumor. Typical sarcomatous metastasis is present in both pulmonary fields.

gram of the chest was normal, and similar study of the elbow region and the humerus failed to show evidence of pathologic change in either soft tissue or bone. On August 15 a block excision of the tumor was performed. The growth was found to extend down to the tendinous insertion of the triceps muscle.

By Sept. 5, 1946, a local recurrence was again present. High voltage roentgen therapy was administered, and the nodule disappeared. Despite this an axillary node was soon noted, and surgical intervention was again advised. Thus on December 23 a radical excision of axillary lymph nodes was performed. Difficulties in healing of the wound were encountered, but it finally healed by Jan. 1, 1947. A second course of radiation was administered.

By April 17, 1947, the mass had again recurred in his arm, and he was coughing. A roentgenogram of the chest (fig. 1) now revealed typical sarcomatous

metastasis. Roentgenotherapy was continued as a palliative measure. On his fourth and last admission to the hospital, Sept. 12, 1947, he had complaints similar to those previously noted, with the addition of dyspnea and occasional hemoptysis. One week after his entrance he experienced severe crushing pain in the chest associated with the feeling of impending death. Diffuse pulmonary rales

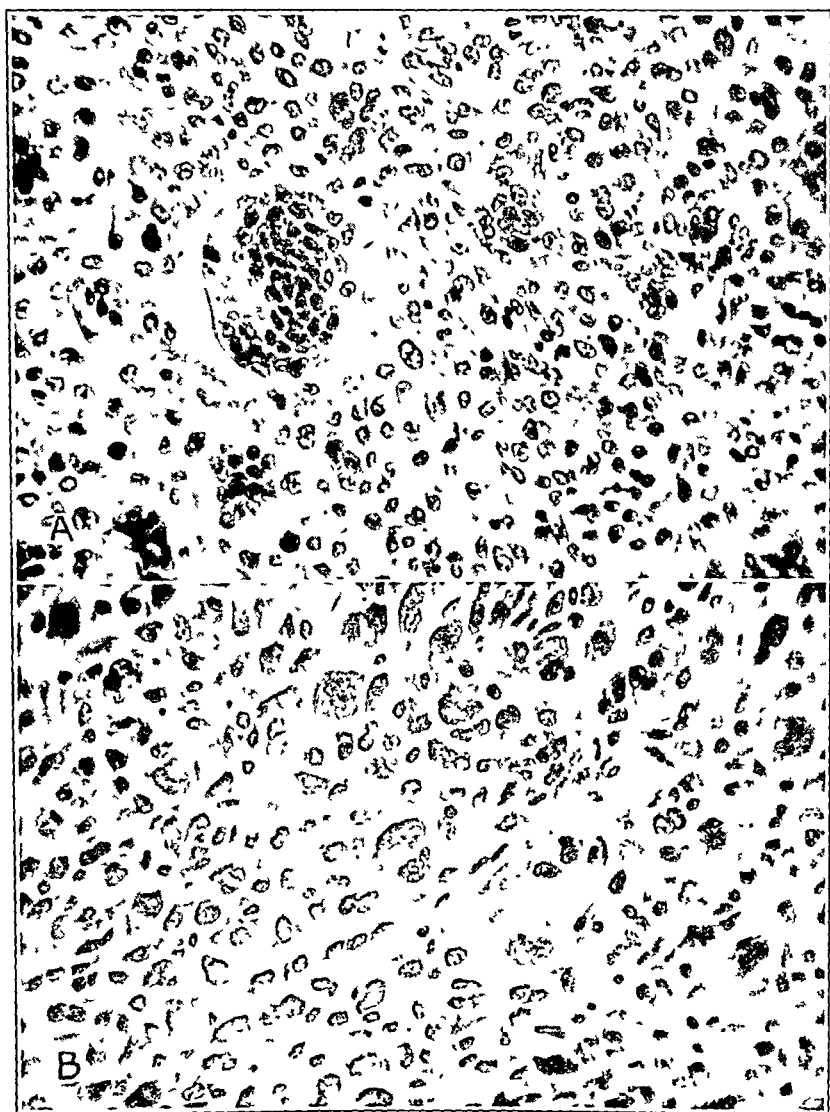


Fig. 2—*A*, photomicrograph of tumor removed at first excision for biopsy (April 4, 1946) showing multinucleate giant cells and polyhedral and spindle-shaped cells with foamy cytoplasm. In numerous areas atypical mitosis is evident. *B*, photomicrograph of tumor removed at third excision (Dec. 23, 1946). The small cellular elements are more pleomorphic and anaplastic. Atypical mitosis is more evident.  $\times 340$ .

became audible, and the respiratory and pulse rates increased. He died on the eleventh day in the hospital, and an autopsy was performed.

The report of the various pathologic examinations is as follows:

Grossly, the specimen removed at the first biopsy, on April 4, 1946, is a well encapsulated tumor, 3 cm. in diameter, consisting of several small cystlike areas which communicate with a large central mass. On section the excised tissue is gray-white, with areas of yellow and areas apparently hemorrhagic.

Microscopically (fig. 2A) the tumor contains four elements, i.e., polyhedral and spindle-shaped cells with foamy cytoplasm, giant cells, interstitial tissue and patches of fibrous tissue and scattered small accumulations of brown pigment. The smaller cellular elements are of polyhedral and spindle shape and reveal moderate pleomorphism and a number of atypical mitotic figures. These cells possess vesicular nuclei with prominent nucleoli. Their cytoplasm is for the most part foamy in appearance. Giant cells, of the multinucleate variety, are scattered

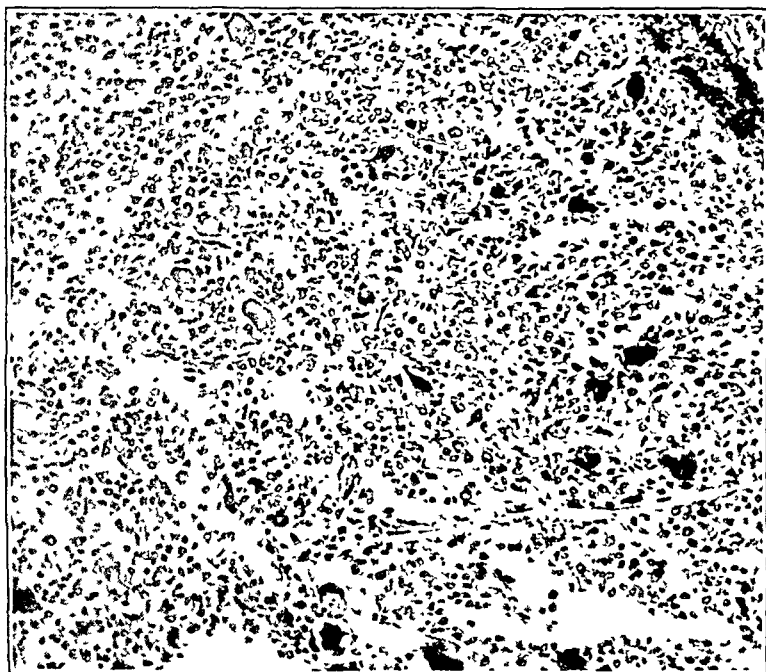


Fig. 3.—Photomicrograph of area of metastasis to lung showing numerous grotesque giant cells, "foam" cells and pleomorphic anaplastic smaller cellular constituents;  $\times 170$ .

throughout. They present a uniform picture and contain numerous equal-sized nuclei, somewhat large and usually grouped centrally within the cytoplasmic mass. Thin strands of fibrous tissue can be distinguished throughout the tumor mass. In some portions larger patches of fibrosis are present. Small areas of brown pigment, obviously hemosiderin, are present in the interstitial tissue, usually within histiocytes. Capillary channels are present throughout but are not conspicuous. Lymphocytes are scantily dispersed throughout.

This tumor morphologically resembles closely a xanthomatous giant cell tumor of tendon sheath origin. However, the stromal cells exhibit somewhat more anaplasia than is usually encountered in these tumors, and there are a number of atypical mitotic figures present. As far as nomenclature is concerned, the term giant cell sarcoma is perhaps best suited in contradistinction to giant cell tumor.

Histologic examination of the specimen removed on Aug. 15, 1946 reveals much more pleomorphism. The giant multinucleated forms show more variation in size, shape and staining qualities as well as numbers of nuclei. The smaller cellular elements are more pleomorphic and anaplastic. Atypical mitosis is more frequent. The majority of the cells are spindle shaped and have either round or elongated nuclei. Others, however, are large and polyhedral or giant and grotesque in character. Some of these cells possess large nuclei with one or many prominent nucleoli. Others contain several to many nuclei and are indistinguishable from the previously described more anaplastic and smaller multinucleate giant cells. A lymphatic channel is seen to be invaded by tumor. This is a definitely malignant tumor, a sarcoma with giant cells.

The tumor removed at the third excision and dissection of the axillary lymph nodes reveals a picture (fig. 2B) similar to that noted in August. However, metastasis to a small lymph node has occurred.

Postmortem examination demonstrates a fungating, dark blue, soft, friable cauliflower mass measuring 12 by 7 cm. on the posterior part of the lower third of the right arm over the insertion of the triceps tendon. Soft bluish tumor nodules, measuring up to 1 cm. in diameter, are scattered over the lateral and medial aspects of the upper third of the right forearm. Similar larger masses are present in the skin of the thoracic wall at the lateral border of the right pectoralis major muscle. The left lung weighs 1,025 Gm. and the right 1,125 Gm. Numerous tumor masses are noted over the surfaces and are palpable within the substance of both. A particularly large mass extends through and into the main left bronchus almost completely occluding this near its origin. From the mucosa in the midportion of the jejunum several dark pink to red nodules project into the lumen. Microscopic sections of all areas of tumor metastasis in the skin, lymph nodes, lungs (fig. 3), bronchi and jejunum are essentially similar to the last biopsy specimen.

#### COMMENT

Much of the difficulty in determining the qualities of giant cell growths in soft tissues apparently stems from inability to classify these tumors properly. Generally they have arisen in tendon or tendon sheath and have conformed to a pattern that has been variously described as xanthoma,<sup>8</sup> a form of synoviomä<sup>4</sup> or giant cell sarcoma.<sup>9</sup>

The question of whether these tumors are malignant or inflammatory has been a chief point of controversy. The concept that they are the former has been based primarily on the fact that infiltrative growth and rapid recurrence have been observed. The lack of metastasis has been taken to indicate the benign nature of the lesion.

Janik,<sup>10</sup> in classifying the sarcomas of tendon sheaths, followed a plan similar to that utilized by Tourneux.<sup>5</sup> In this system the sarcomas are divided into two varieties: (a) the sarcoma gigantocellulare (mye-

8. Galloway, J. D. H.; Broders, A. C., and Ghormley, R. K.: Xanthoma of Tendon Sheaths and Synovial Membranes, *Arch. Surg.* **40**:485-538 (March) 1940.

9. Rags, A. B., and Shiveley, F. L.: Further Observations on Benign Giant Cell Tumors of the Tendon Sheaths, *Ann. Surg.* **109**:632-640 (April) 1939.

10. Janik, A.: Tumors of Tendon Sheaths, *Ann. Surg.* **85**:897-911 (June) 1927.



loma or xanthosarcoma), a benign, lobulated, well encapsulated growth with giant cells, lipid cells and blood pigments and (b) the sarcoma fusocellulare and glubocellulare, a malignant neoplasm in which the giant cells and lipid cells are absent. The latter growth would be akin to the usually described fibrosarcoma.

Other authors<sup>11</sup> more recently have attempted a classification of these lesions based on the origin of the stromal cells. King<sup>6</sup> expressed the belief that the stromal cells are of far greater importance in determining the characteristics of the tumor than the presence of giant cells or xanthoma-like cells. In his concept the giant cells are of the foreign body type and are due to tissue deposits of cholesterol. The foam cells, too, are incidental phagocytes. He concluded that the tendon sheath tumors are neoplastic. Many, though, are of a low grade malignant type with additional inflammatory reaction. The benign forms of growth possess spindle and spheroidal cells, a moderate number of mitotic figures and occasional tissue clefts. The more malignant varieties are like the benign, but the cells are more irregular and embryonic. Many mitotic figures may be seen in these instances. No cases are reported in which this more malignant variety metastasized.

Smith<sup>12</sup> has observed that certain malignant tumors arising from serous bursas, joints and tendon sheaths seemed to possess features in common. The term synovioma was applied to them with the understanding that these growths took origin from the synovial lining cells, the outer fibrous synovial tissue or portions of both of these.

It is considered by many that the benign lesions of tendons likewise are related to the synovia. Berger,<sup>4</sup> for example, stated that the xanthomatous giant cell tumor is related to synovial tumors. He stressed the fact that these giant cell lesions are the result of the histiocytic potentialities of synovial tissue, which may dominate and suppress the endothelial potentialities. The xanthomatous giant cell tumor may thus be considered a synovial histiocytoma.

The term synovial sarcoma has been used by many.<sup>13</sup> It was observed by De Santo and others<sup>7</sup> that these tumors were characterized by (1) endothelial features such as glandlike spaces with mucin, villi and flat epithelium and (2) histiocytic features such as (a) reticulum cell sarcoma-like aspects with round or oval nuclei, (b) giant cells and (c) xanthoma cells similar to those in benign xanthomatous giant cell tumors.

It is the impression of these authors<sup>7</sup> that all synovial sarcomas may be malignant but not equally so. The least malignant show histio-

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11. Berger<sup>4</sup>. King<sup>6</sup>. De Santo, Tennant and Rosahn.<sup>7</sup>

12. Smith, L. W.: Synoviomata, *Am. J. Path.* 3:355-364 (July) 1927.

13. (a) Haagensen, C. D., and Stout, A. P.: Synovial Sarcoma, *Ann. Surg.* 120:826-842 (Dec.) 1944. (b) Berger.<sup>4</sup> (c) De Santo, Tennant and Rosahn.<sup>7</sup>

cytic differentiation and resemble the xanthomatous giant cell tumor. The next most malignant are those with glandlike spaces (which would appear to be like synovioma). The most malignant resemble fibrosarcoma. In this study there were also no reported instances of metastasis from the least malignant variety. However, an intra-articular synovioma (case 11) was described in which areas were found to resemble the benign form of giant cell tendon tumor. This growth eventually metastasized.

Haagensen and Stout,<sup>13a</sup> on the other hand, distinguished between synovial sarcomas and the benign lesions such as xanthomatous giant cell tumors. They adhered to the concept that synovial sarcomas must possess two elements: (1) a fibrosarcomatous element, with spindle cells and (2) a synovial element, often with tissue clefts, villous formation and mucin.

Foot,<sup>14</sup> in discussing tumors of striated muscle, called attention to the fact that the nonmalignant varieties may simulate xanthoma both grossly and microscopically. These myeloblastic tumors have elongated cells, often multinucleated, and usually bear no evidence of intracellular striations. However, the cytoplasm of the giant cells is distinctively acidophilic.

Geschickter and Copeland<sup>15</sup> stated the belief that these tumors are derived from sesamoid bones. The peritendinous portion of the triceps muscle would seemingly be a more logical site in the present case. It is interesting to theorize that despite the absence of synovial tissue in such a flat tendon there is nevertheless a relation between the cellular prototypes which make up the covering of the tendon and those of the synovial structures, as in the hands and feet. The tumor cells could be related to these.

In the case presented here the tumor possessed features which under any classification would have placed it in the more benign variety of lesions. The presence of giant cells and numerous foam cells and the general absence of tissue clefts would seemingly have indicated a benign lesion. Likewise these factors would have differentiated it from the usually malignant synoviomias. However, various features were noted, even initially, which made the pathologists exceedingly wary of the eventual prognosis. Among these were the fact that far more atypical mitotic figures were noted than are seen in the usual benign giant cell lesion. Secondly, there were numerous examples of pleomorphism and grotesque character of the dividing cells. In addition the location

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14. Foot, N. C.: *Pathology in Surgery*, Philadelphia, J. B. Lippincott Company, 1945.

15. Geschickter, C. F., and Copeland, M. M.: *Tumors of Bone*, New York City, The Lancaster Press, 1936, p. 736.

of the tumor was unusual. Lastly, the rapidity of recurrence pointed toward an eventually poor outcome.

Of further interest is the fact that the pathologists believed that the picture terminally could best be described as one of highly malignant sarcoma with giant cells. However, review of the microscopic sections of the surgical and postmortem specimens still gave the impression, even in retrospect, that the original lesion was essentially identical with xanthomatous giant cell tumor.

In the attempt to form a basis of treatment, it cannot be overlooked that in over 100 cases of xanthomatous giant cell growths noted in the literature there have been, with the possible exception of the cases cited by Tourneux<sup>6</sup> and De Santo and others,<sup>7</sup> no definite evidences of metastasis. Therefore it would seem that for giant cell lesions, and particularly those in the usual locations on the tendons of the hands or feet, a local excision would be indicated. In this regard due emphasis must be given to the histologic nature of the lesion. If the stromal cells possess more mitosis than usual, a more bizarre cell pattern or perhaps unusually large numbers of clefts, then more radical excision and dissection of regional lymph nodes are indicated. Likewise, if the giant cells possess striated myeloblastic character, more extensive measures of therapy would be recommended.

Recurrence of growth following surgical extirpation similarly indicates a need for more energetic treatment. The extent of this must depend not only on the original pathologic findings in serial section but also on the character of the growth as noted in reexcision. In cases in which there are synovioma-like features amputative procedures have been recommended by many.<sup>13a, c</sup> Roentgen therapy has been of little avail in preventing recurrence of these tumors.

#### SUMMARY

An instance of malignant, soft tissue, xanthomatous giant cell tumor has been reported. This growth originated in the peritendinous portion of the triceps muscle and eventually metastasized widely to the regional lymph nodes, lungs and abdominal viscera. The literature bearing on the subject has been reviewed, and emphasis has been placed on the rarity of such a lesion and on the problems of classification and therapy.

## GRANULOMAS OF LARGE SIZE CAUSED BY IMPLANTATION OF TALCUM (TALCUM SARCOIDS)

G. E. GRUENFELD, M.D.

ST. LOUIS

IN MOST hospitals the preparation of rubber gloves involves the use of talcum powder, which is the finely pulverized mineral talc so widely used in industry and in cosmetic preparations. Chemically it consists of a combination of hydrous magnesium silicate,  $\text{H}_2\text{Mg}_3\text{Si}_4\text{O}_{12}$  (chemically pure talc), calcium magnesium carbonate, calcium magnesium silicate and other related substances in varying proportions. Its usefulness for the servicing of surgical rubber gloves is apparently based on the following properties: (a) It withstands easily the heat of the sterilization process. (b) It absorbs films of moisture from rubber and skin. (c) It eases friction between rubber and skin surfaces by a ball-bearing effect of the minute powder particles. Other substances which could be used for the same purpose have apparently not been widely accepted, so that the field today is still left almost exclusively to talcum powder.

While much fault cannot be found with the purely physical properties of talcum powder, it needs to be emphasized that in contact with living tissue it is, not infrequently, productive of serious reactions in the form of chronic inflammations or tumefactions. This statement might come as a surprise to many surgeons who, during their long and busy careers, have used talcum powder in and on rubber gloves seemingly with complete satisfaction and without untoward results. But there is no question that in some circumstances, at present unknown in their portent, disease processes might be started by the insemination of glove powder into the tissues exposed by surgical intervention. This refers not to any unusually heavy contamination with measurable quantities of powder, but to the minutest, merely microscopic retentions of talcum particles unavoidable even if the surgical team rinses its gloves meticulously after slipping them on.

The sense of security which surgeons derive from the use of rubber gloves has been disturbed by recent warning reports. (See Antopol,<sup>1</sup>

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From the Surgical Services of Barnard Free Skin and Cancer Hospital and the Jewish Hospital of St. Louis.

1. Antopol, W.: Lycopodium Granuloma, Arch. Path. 16:326 (Sept.) 1933.

Owen,<sup>2</sup> Fienberg,<sup>3</sup> German,<sup>4</sup> de Savitsch,<sup>5</sup> Byron and Welch,<sup>6</sup> McCormick and Ramsey,<sup>7</sup> Ramsey,<sup>8</sup> Seelig, Verda and Kidd,<sup>9</sup> Lichtman and others,<sup>10</sup> Eiseman, Seelig and Womack,<sup>11</sup> Roberts<sup>12</sup> and Klemm.<sup>13</sup>) It is not without interest to note that although the evil of irritating dusting powders like lycopodium was described over fifty years ago, it was not until the past few years that any insistence was laid on the necessity of banning the use of talc during surgical procedures. In a recent contribution from the Mayo Clinic, the categorical statement is made that "talcum must go." Seelig and his co-workers, who were the first to attack the problem of finding a substitute for talcum, are still engaged in a search for a dependable and reliable one.

It is my purpose to call attention again to a potential hazard ascribable to a routine surgical technic which is so generally and so erroneously accepted as being entirely satisfactory. I shall take as an example the following incident:

A young woman, aged 21, noticed a painless swelling grown to a conspicuous size in the right lower region of the abdomen for three weeks before presenting herself. Eleven years previously, at the age of 10, she had undergone an appendectomy, a short McBurney incision being used. The operative scar was normal, and she stated that her postoperative recovery had been prompt and that no disturbance in the region of the wound had ever been noticed before. The tumor, so recently observed, developed beneath the operative scar, evidently in the deeper layers of the abdominal wall but leaving uninvolved the overlying skin. This was considerably elevated by the nodular mass, which measured, at the time of her admission to the hospital, approximately 12 by 5 cm. In the opinion of her

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2. Owen, M.: Peritoneal Response to Glove Powder Containing Talcum, *Texas State J. Med.* **32**:482, 1936.

3. Fienberg, Q.: Talcum Powder Granuloma, *Arch. Path.* **24**:36 (July) 1937.

4. German, W.: Dusting Powder Granulomas Following Surgery, *Surg., Gynec. & Obst.* **76**:501, 1943.

5. de Savitsch, E.: Granuloma Resulting from Penetration of Talcum Powder, *M. Ann. District of Columbia* **9**:169, 1940.

6. Byron, F. X., and Welch, C. S.: Complication from Use of Glove Powder, *Surgery* **10**:766, 1941.

7. McCormick, E. J., and Ramsey, T. L.: Postoperative Peritoneal Granulomatous Inflammation Caused by Magnesium Silicate, *J. A. M. A.* **116**:817 (March 1) 1941.

8. Ramsey, T. L.: Magnesium Silicate Granuloma, *Am. J. Clin. Path.* **12**:553, 1942.

9. Seelig, M. G.; Verda, D. J., and Kidd, F. H.: The Talcum Powder Problem in Surgery, *J. A. M. A.* **123**:950 (Dec. 11) 1943.

10. Lichtman, A. L.; McDonald, J. R.; Dixon, C. F., and Mann, F. C.: Talcum Granulomas, *Surg., Gynec. & Obst.* **83**:531, 1946.

11. Eiseman, B.; Seelig, M. G., and Womack, N.: Talcum Powder Granuloma: A Frequent and Serious Post Operative Complication, *Ann. Surg.* **126**:820, 1947.

12. Roberts, G. B. S.: Granuloma of the Fallopian Tube Due to Surgical Glove Talcum, *Brit. J. Surg.* **34**:417, 1947.

13. Klemm, C.: Foreign Body Granulomatosis of Peritoneum Caused by Talcum Powder, abstracted *Helvet. chir. acta* **14**:181, 1947.

physician the mass had been expanding in size during the preceding few weeks of observation, and therefore her statement about its short duration was probably correct. There was no tenderness; the surface of the mass was nodular, its consistency firm and its delineation from the surrounding subcutaneous tissue definite. The base of the tumor was broadly attached to the aponeurosis of the external oblique muscle. There was no fever, but the white blood cell count was increased to 12,000.

With the differential diagnosis of granuloma or sarcoma, the mass was excised with a small ellipse of skin, the appendectomy scar forming its axis. Since the gross examination of the tissue suggested sarcoma rather than inflammation, the incision was enlarged and a generous block excision was done including the adjacent subcutaneous fat and the tumor base consisting of the external oblique aponeurosis. The exposed portions of rectus and oblique abdominal musculature appeared uninvaded. Closure of skin could be accomplished by flexing the thigh. The subcutaneous space was drained through a stab wound and a compressing hip spica bandage applied. The postoperative course was uneventful. The abdominal wall appeared firm for some time in spite of the loss of fascia. However, four years after the operation a slight incisional hernia had established itself.

The specimen contained a uniformly hard induration diffusely originating from the aponeurotic layer but distinctly outlined against the subcutis, into which it projected with nodular prominences. The configuration and consistency of the tumor suggested sarcoma.

The microscopic sections revealed that the mass was composed of closely spaced small tubercles, the smallest about the size of a kidney glomerulus and others four to ten times larger. There were usually only slender strands of cellular connective tissue delineating the well rounded tubercles. The tubercle-like accumulations of cells extended diffusely into the dense sheet of connective tissue representing the removed piece of aponeurosis and in a like manner into the subcutaneous fat, but in this layer there was, at times, by way of encapsulation, a thin barrier of connective tissue laid down between the most peripheral tubercles and the fatty tissue. Throughout the mass and the adjacent adipose tissue, fair-sized blood vessels were noticeable with patent lumens and barely any inflammatory reaction in their walls.

The individual tubercles were composed predominantly of epithelioid cells which showed no inclination toward caseous necrosis. Round cells or lymphocytes were scarce and leukocytes absent. Many of the epithelioid cells were fused to form multinucleated giant cells with preserved tinctorial behavior, while other giant cells exhibited deeper-staining cytoplasm and nucleoplasm and therefore could be of a different origin. Significantly, small needle-like inclusions were found in many of the dark-staining giant cells. This finding, together with the fact that caseation was absent, led to the conclusion that a foreign body granuloma was being dealt with.

My colleagues and I were at first at a loss to determine the exact nature of the foreign body reaction until, stimulated by the publications of the group of workers at the Barnard Free Skin and Cancer Hospital, we studied our sections with a polarizing microscope. It immediately became clear that we were dealing with a foreign body reaction due to talcum. Subsequently, Dr. Werner, of the Department of Geology, Washington University, examined the section with special equipment and came to the conclusion that the crystalline foreign bodies found disseminated throughout the section and particularly contained within the giant cells were optically anisotropic with parallel extinction. "They looked and behaved like crystals of actinolite-tremolite, which is calcium magnesium silicate and frequently found in talcum powder as 'impurities.'"

## COMMENT

The implantation of infinitesimal quantities of talcum into or onto human and animal tissue has been found to provoke inflammatory reactions varying greatly in intensity and persistency. It is obscure what factors are responsible for this variability of the tissue response, which is in contrast to the rather stereotyped histologic finding, namely, foreign body giant cells containing microcrystals singly or grouped in small clusters. When the tissue sections are viewed with polarized light the foreign substance can be identified with some facility; "the silicate crystals will be seen to stand out in brilliant illuminations as an electric sign in a night sky" (German). One has to defer, however, to expert petrographic analysis of the crystals in order to ascertain their chemical nature. One should also be aware of the fact that cellulose fibers are similarly refractile to polarized light.

The clinical pathologic pictures produced by talcum do not lend themselves easily to a general description. I propose therefore to recapitulate briefly what is generally known about the consequences of talcum irritations under five headings, a nosologic division which is admittedly arbitrary.

1. *Insemination of Talcum Without Apparent Tissue Reaction.*—Probably an appreciable number of contacts between talc and living tissue remain uncomplicated by visible clinical reaction. Since tissues are rarely examined histologically unless some gross changes arrest the attention, little is known about the prevalence or relative absence of microscopic tissue responses. From the observations reported in the following paragraph it seems likely that absolute inertia of the tissue defense against talc probably never prevails.

2. *Reactions of the Peritoneal Cavity to Talcum.*—Experiments on a smaller scale have been conducted by German<sup>4</sup> and mass experiments by Schultz and Williams,<sup>14</sup> Miller and Sayres<sup>15</sup> and Owen.<sup>2</sup> Almost regularly, the instillations of weak suspensions of talcum in isotonic sodium chloride solution or the sparse dusting of the visceral peritoneum with the dry powder would produce visible reactions. It remains, naturally, impossible to ascertain whether each and every point of contact between the mineral and the peritoneum became the site of a tissue reaction. The cumulative result of the experiments seems to be that talcum particles produce a visible nodule, which microscopically is represented by a focus of cellular accumulation in the serosa and subserosa engulfing the crystals. Macrophages and foreign body giant cells were found to contain the microcrystals intra-

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14. Schultz, R. Z., and Williams, C. R.: Commercial Talcum: Animal and Mineralogic Studies, *J. Indust. Hyg. & Toxicol.* **24**:75, 1942.

15. Miller, J. W., and Sayres, R. R.: The Physiological Response of Peritoneal Tissue to Certain Industrial and Pure Mineral Dusts, *Pub. Health Rep.* **51**:1677, 1936.

cellularly. True granuloma formation, i. e., a clustering of such foci or the formation of adhesions, was not noted. As a matter of fact, German<sup>4</sup> emphasized the neat restoration of the serosal surface at the portal of entry of talcum into the peritoneum. Concerning the persistence of these talc nodules, long range experiments extending observations over a period of two years after exposure indicate a tendency toward a rather complete resolution of the cellular accumulations. In no instance was a progressive disease process found, which is of interest in connection with the case report given previously.

In the realm of human pathology the role of talcum as a provoker of significant pathologic changes in the peritoneal cavity cannot be doubted any more. Two types of peritoneal reactions have been ascribed to it: (a) nodular reaction grossly simulating tuberculosis or carcinomatosis and (b) adhesive peritonitis. Concerning the former, it may be stated with certainty that the etiologic role of the mineral is exclusive, since the findings conform with experimental observations. The dry, adhesive peritonitis type of reaction, on the other hand, is more difficult to evaluate. Since it is probable that similar peritonitic reactions have occurred without talcum, the etiologic role of this foreign body can be only suspected and may be merely a contributory one in persons who have this type of excessive peritoneal response. The absence of progressive adhesive inflammation of the peritoneum in the numerous experiments on animals cannot be overlooked, and it is questionable whether Bethune's production of adhesive pleuritis with talcum poudrage can be adduced in confirmation since he used massive quantities for his procedure.

Regardless of whether talc plays an exclusive or an auxiliary role in the production of postoperative adhesions in a given case, due consideration must be given this potentiality not only in the pathologic diagnosis but also in prophylaxis. German and, especially, Seelig and his co-workers<sup>16</sup> have emphasized this aspect, and the latter have justly called for the banishment of talcum from the operating room and the substitution of tartrate powder and later of special starches sufficiently heat resistant for use in the autoclave.<sup>17</sup>

3. *Injections of Talcum into Ocular Tissues.*—Irrigations of the anterior chamber of the eyes of small experimental animals and the injection into the sclera of talcum suspensions were done by Chamlin.<sup>18</sup>

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16. Seelig, M. G.: Dangers of Talcum in the Peritoneal Cavity, J. A. M. A. **121**:1304 (April 17) 1943; Dusting Powder for Rubber Gloves, *ibid.* **123**:113 (Sept. 11) 1943; Dusting Powder for Surgical Gloves, *ibid.* **125**:1208 (Aug. 26) 1944.

17. Lee and Lehman, too, have recently reported that a certain modified starch could be used not only as a convenient but also as a safer glove powder (Surg., Gynec. & Obst. **84**:689, 1947).

18. Chamlin, M.: Effect of Talc in Ocular Surgery, Arch. Ophth. **34**:369 (Nov.-Dec.) 1945.



In the majority of eyes so treated inflammatory reactions featuring foreign body giant cells developed. On the basis of these results, Chamlin advocates the careful rinsing of the rubber gloves in a stream of sterile water. Seelig<sup>19</sup> has told me that a few milligrams of talcum injected by him into the anterior chamber of a rabbit's eyes sets up a violent reaction that leads to loss of sight.

4. *Talcum Granulomas in Connection with Foci of Suppuration.*—A histologic study of suppurating postoperative wounds and sinuses which makes use of the technic of polarized light will uncover in some the presence of talcum crystals within foreign body giant cells. Such foci of talc reaction with fistulous connection to the outside have been found in parenchymatous organs, in muscles and in the subcutis. For the purpose of emphasis there is selected from the several cases reported in the literature one of German's<sup>4</sup> in which talc granulomas developed in a circumcision wound. A cicatricial phimosis resulted and necessitated a second circumcision. The combination of chronic suppuration and talcum reaction appears as a typical disease process, easily acceptable as a parallel of tissue reactions to other foreign substances. The combination of the two factors, infection and foreign body, makes it impossible to decide which of them plays the leading role. It is possible that the incidence of infection gave rise to the inflammatory reactions, which subsequently focused also around the primarily inert mineral particles. Equally plausible is it to assume that the mineral material irritated the tissues to the extent that they were unable to cope with the contaminating bacteria and promoted the "taking" or the chronicity of the infection.

5. *The Sarcoid Talcum Reactions.*—Although the term sarcoid has been applied by prior observers, apologies are here offered for its lack of scientific distinctiveness. In consulting medical dictionaries, one learns that this expression does not impart a definite etiologic or histogenetic meaning. It seems that the term "sarcoid" was originally used to describe the pathologic tissues which grossly resembled sarcomas. Some, or most, of such sarcoid tumefactions were found microscopically to be conglomerations of tubercle-like inflammatory foci. At the present time only the diseases named after Boeck and Darier and Roussy, which resemble sarcoma in scarcely any respect but which have a histologic pattern of giant cell tubercles, are officially termed "sarcoid." The latter application is the only recognized modern use of the term sarcoid. In its original descriptive meaning it is no longer found in the nomenclature of diseases. This is somewhat regrettable since the granulomas provoked by talcum trisilicate sometimes assume a gross appearance simulating a sarcomatous new growth. Microscopically, they are indeed classic examples of giant cell tubercles forming large conglomerations. It is therefore both from the gross

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19. Seelig, M. G.: Personal communication to the author.

and the microscopic observations that license is taken to call these specific forms of talcum reactions "sarcoids."

In contrast to all observations pertaining to pathologic changes in general produced by talcum experimentally, the talcum sarcoid observed clinically has a lag period, frequently covering years, and when once started may exhibit progressive tendencies which vie with those of infections.

Case reports which exemplify these sarcoid reactions are described by various authors. In Fienberg's<sup>3</sup> case a tumor developed in the fascia of abdominal muscles six years after an appendectomy. Byron and Welch<sup>6</sup> described a tumor measuring 2.5 by 4 cm. which developed in a laparotomy scar five years after a hysterectomy. Lichtman and others<sup>10</sup> mentioned in their extensive review a "sarcoid" of the gallbladder found eleven years after cholecystostomy, the talcum being presumably introduced by the drainage tube. German<sup>20</sup> described as "lupoid-sarcoid reaction" a nodule 2 cm. in diameter developing after fifteen years in a scalp wound which originally had healed by primary intention. Crystals of silica were found engulfed by foreign body giant cells. (In this case, however, the agent was not talc.)

Evidently these exquisitely tumefacient talcum reactions are much rarer than peritoneal talcum nodules or adhesions or talcum foci in a sinus after operation. This infrequency with which the cause (insemination of talc) produces the effect (sarcoid) suggests that the relationship is not a simple one and of necessity involves several unknown factors. As far as I am aware, no attempt has been made to elucidate them. At present any explanation would be only speculative and could at best merely outline possible approaches to the problem.

In making allowance for the great time lag in the development of these sarcoid reactions, one may be tempted to liken them to the fibrosis produced by silica, a related compound, in pulmonary tissue. This noxa is notorious for the delay of pathologic changes. This has been tentatively explained as due to a slow leaching of the silica by reagents produced secondarily in the tissues, new silica compounds thus formed going eventually into solution and irritating the tissues and eliciting a productive type of inflammation. Cases in which pulmonary fibrosis does not supervene evidently exemplify the innocuousness of chemically unaltered silica. A similar mechanism could be assumed operative in cases of talcum sarcoid with the implication that the solvents for the various silicates contained in industrial talcum powders are produced in the human body much less frequently than those leaching silica.

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20. German, W.: Lupoid-Sarcoid Reaction Induced by Foreign Body (Silica), *Am. J. Clin. Path.* **10**:245, 1940.

However, this is not the only hypothesis suggesting itself. One may propose that the mineral dust deposits in the tissues be considered as a localizing agent for an infectious noxa which, while gaining access to the focus on a subsequent occasion, acts as the real and immediate pathogen. In the field of experimental bacteriology it is a well known phenomenon that a general infection can be made to localize in areas predetermined by the injection of a foreign substance like kieselguhr.

If this theory should appear unattractive, reference may be made to some now almost forgotten sequelae of foreign body implantation. When silk sutures of heavier grades were more commonly used, progressive inflammatory tumors were known to develop in some instances many years after operation, especially after herniotomies (so-called Schloffer tumors<sup>21</sup>). The nucleus of these swellings was usually a minute abscess around a silk thread. In a similar manner, i. e., after long lag periods, huge swellings of the omentum (described by Braun) have developed after its partial resection with the aid of silk sutures. In order to perturb any one who might contend that this omentitis of Braun is simply a protracted surgical bacterial contamination with late rekindled inflammation, Probstein<sup>22</sup> reported a case of extensive omentitis in which no laparotomy or trauma preceded the infection.

Accordingly, the logical possibilities to explain the talcum sarcoid and especially its conspicuous lag period narrow down to three, with a free choice between them: 1. In some, but only comparatively few, patients "antibodies" to one of the silicates contained in industrial talcum eventually develop. The interaction between the talcum and the antigen elicits a tissue response in the form of giant cell tubercles. 2. The minute mineral deposits of talcum act as "localizers" for certain unknown bacterial or viral organisms circulating otherwise harmlessly in the body. 3. The mineral deposits prevent the elimination of bacterial or viral contaminations incident to the surgical exposure. Clinically perceptible inflammations develop when the dormant organisms become virulent.

#### SUMMARY

The nefarious potentialities of talcum glove powder have only recently been recognized. One of the rarer postoperative complications attributable to minute quantities of this material is the development of a sizable hard tumor-like swelling as late as ten years or more after the surgical intervention.

The long latency period and the size of this "sarcoid" foreign body reaction distinguish it from other, more common, talcum reactions.

21. Roska, L.: Schloffer Tumor of the Abdominal Wall, *Zentralbl. f. Chir.* **66**:1757, 1939. Schloffer, H.: Ueber chronisch entzuendliche Bauchdecken-geschwuelste nach Bauch-operationen, *Verhandl. d. deutsch. Gesellsch. f. Chir.* **37**: 229, 1908.

22. Probstein, J. G.: Recurrent Omental Hypertrophy, *Am. J. Surg.* **16**:50, 1932.

# PSEUDOCYST OF THE LIVER

## Report of a Case

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AND

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POST-TRAUMATIC bile cysts of the liver are extremely rare. A search of the literature reveals only 4 cases which have been recorded.<sup>1</sup> The nonparasitic bile cyst could properly be classified as a pseudocyst by comparing it with the pseudocyst of the pancreas, which does not have an epithelial lining. Nonparasitic cysts of the liver, which are not the direct result of trauma, are not so rare. Davis<sup>2</sup> reviewed the literature on nonparasitic cysts in 1937 and gathered 499 cases, of which 241 were classified as cases of cystic disease of the liver with multiple cysts, 187 as cases of solitary unilocular cysts and 20 as cases of solitary and monolocular cysts. The remaining 51 were not classified. Clagett and Hawkins<sup>3</sup> have recently reported the successful removal of a multilocular cyst by extirpation of the entire left lobe of the liver.

## REPORT OF A CASE

A white girl aged 3 was first seen in the John Sealy Hospital on Sept. 5, 1947, at 10 a. m. She had just been run down by an automobile. Whether or not the vehicle passed over the child's body could not be determined. Examination revealed a child in a moderate degree of shock; there were swelling and edema of the left side of the face. Some rales could be heard at the right base. There was no dulness. Abdominal tenderness and rigidity were generalized, but they were more pronounced on the right side. There was a small tear in the perineum. There was roentgenologic evidence of increased bronchovascular markings in

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From the Surgical Research Laboratory and the Department of Surgery, University of Texas, Medical Branch.

1. Curran, J. F., and Goodale, R. H.: Traumatic Bile Cyst of Liver, *New England J. Med.* **207**:1192, 1932. Whipple, C.: A Case of Traumatic Rupture of the Liver: Formation of Cystic Swelling Containing Bile-Stained Fluid; Incision and Drainage; Recovery, *Lancet* **1**:719, 1898. Aldridge, A. R.: Rupture of the Liver: Formation of Cystic Swelling Containing Bile-Stained Fluid, *ibid.* **1**:1616, 1898. McQuillan, A. H.: Traumatic Bile Cyst, *J. Maine M. A.* **19**:193, 1928.

2. Davis, C. R.: Non-Parasitic Cyst of the Liver, *Am. J. Surg.* **35**:590, 1947.

3. Clagett, O. T., and Hawkins, W. J.: Cystic Disease of the Liver, *Ann Surg.* **123**:111, 1946.

both lungs. In the right lung there were mottled shadows of increased density which were suggestive of alveolar hemorrhage or possibly bronchopneumonia. There was an incomplete linear fracture of the right wing of the ilium. The temperature was 101 F., the pulse rate 140, the respiratory rate 40 and the blood pressure 80 systolic and 40 diastolic. The child responded rapidly to expectant treatment. She was afebrile on the fourth day of hospitalization and was dismissed on the eleventh day. The following day the patient was returned to the hospital because of swelling of the abdomen. At this time she had a temperature of 100.2 F. The abdomen was distended and tender. She ate poorly. There was no evidence of obstruction of the gastrointestinal tract, and she had not vomited. The abdominal tenderness was still primarily on the right side. The condition slowly resolved itself, and the patient was dismissed from the hospital five days later. Four days later she vomited and was readmitted to the hospital. Abdominal distention had continued. She had a temperature of 101 F., a pulse rate of 120 and a blood pressure of 90 systolic and 60 diastolic. She was eating well and had received daily enemas. The abdomen was protuberant, with tenderness to palpation in both upper quadrants. There was moderate muscle spasm over the entire abdomen. Intra-abdominal viscera could not be felt. On the sixth day of this stay in the hospital the abdomen became distended, and for the first time a large epigastric mass about 8 cm. in diameter was palpable. This mass was dull to percussion. The nonprotein nitrogen was 22 mg. per hundred cubic centimeters, the serum amylase 60 units and the reaction to the cephalin flocculation test 2 plus in 24 and 48 hours. The blood count showed 3,850,000 red cells and 16,400 leukocytes, with a differential count of 61 per cent polymorphonuclear cells, of which 52 per cent were adult forms, 36 per cent lymphocytes, 2 per cent monocytes and 1 per cent basophils. The sedimentation rate was 42 mm. in 1 hour. Repeated determinations of the serum amylase level showed 57 units. Four days later roentgenologic examination revealed the stomach to be pushed to the left and downward. A tentative diagnosis of pseudocyst of the pancreas was made. Intravenous urographic examination showed the kidneys to be normal.

On the following day the patient was examined through a short, transverse incision above the umbilicus and to the left. A cystic mass presented itself in the wound, from which clear bile could be aspirated. The cyst was about 10 cm. in diameter and occupied the anterior surface of the left lobe of the liver. It contained approximately 150 cc. of clear bile and was just beneath the capsule of the liver. It was excised. The cyst wall was easily stripped from the surface of the liver. At one point on the surface of the liver there was an opening about 2 mm. in diameter from which clear bile issued. This opening was closed with a purse string suture of 2-0 chromic surgical gut. Exploration revealed no other abnormalities of the intra-abdominal contents, and the abdomen was closed without drainage. For about ten days postoperatively there was abdominal distention, with some vomiting. Thereafter the course was uneventful, and the patient was dismissed from the hospital on the twentieth postoperative day and has continued to be well. Microscopically, the inner surface of the cyst wall was composed of dense fibrous connective tissue. There was no true epithelial lining. In the outer layers of the wall the tissue was loose and edematous and contained numerous engorged blood vessels. There was abundant collagen formation. The essential features were those of marked connective tissue hyperplasia.

# COMMENT

The development of the traumatic bile cyst does not follow any clear pattern, and there is not a definite train of signs or symptoms. There is abdominal distention, with tenderness. The appetite may be poor. There is prostration, with occasional low grade fever. Sometimes vomiting of mild degree occurs and finally localization of tenderness over the cystic mass. In the reported cases the mass had developed within one to five weeks. In this case it was first palpable one month after the injury. In no instance was a correct diagnosis made pre-operatively. In all probability, traumatic bile cysts of the liver should be considered as primary lesions and be defined as a pseudocyst of the liver similar to the pseudocyst of the pancreas. It is conceivable that a pseudocyst of the liver could arise after the resolution of a deep abscess in the liver under the influence of chemotherapy and antibiotic treatment or after the resolution of a large intrahepatic hematoma.

# SUMMARY

The fifth case of nonparasitic cyst of the liver following trauma is presented, and it is proposed that these bile cysts be known as pseudocysts of the liver. The maximum postoperative rectal temperature was 101 F. It returned to normal on the second postoperative day and remained normal throughout the patient's stay in the hospital.

## ISLET CELL TUMOR OF THE PANCREAS

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THE PATIENT whose history is reported in this communication presented a tumor of islet tissue which was of interest for the following reasons: It did not produce hyperinsulinism; it was unusually large in size, and it had undergone cystic degeneration, which is rare in growths of this type.

### REPORT OF A CASE

*History.*—On May 12, 1942, a 65 year old housewife was admitted to the Roosevelt Hospital complaining of pain in the left upper region of the abdomen. Except for a hysterectomy for uterine fibroids twenty years previously, there had been no medical or surgical illnesses of any significance. In April 1942, about four weeks prior to her admission, the patient began to have a constant dull ache in the epigastrium and left upper quadrant. Within a few days she began to have occasional vomiting, which soon became persistent. During the ensuing three weeks she had retained no solid food whatever, and for several days prior to her admission she had been vomiting liquid feedings as well. The stools and urine had been scanty but normal in color. She had had no chills or fever. The pain had gradually become more severe and seemed to have become definitely localized in the left upper quadrant and left subcostal area.

*Physical Examination.*—Examination revealed an obese elderly white woman 65 years of age, weighing 168 pounds (76.2 Kg.), who was acutely ill. The temperature was 99 F., the pulse rate 68 and the respiratory rate 20. The blood pressure was 130 systolic and 70 diastolic. The scleras were not discolored. The tongue was thick and dry. There were no palpable cervical or supraclavicular nodes. The lungs were clear. The heart was slightly enlarged to the left, and the sounds were of good quality, with no murmurs. The abdomen showed a well healed median suprapubic scar. In the left upper quadrant there was a smooth round mass about 12 cm. in diameter, which was slightly tender and which appeared to be fixed. It did not move with respiration. The liver and spleen were not palpable. The extremities were normal.

*Clinical and Laboratory Studies.*—The urine and blood were entirely normal. Intravenous pyelograms showed good filling of the pelves and calices, with no evidence of dilatation or pressure defect. Both ureters were well outlined and showed no displacement.

After four days of observation and preparation, including blood transfusions and infusions of dextrose and isotonic sodium chloride solution, the patient was operated on, on May 16, 1942. The preoperative diagnosis was tumor of the pancreas.

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From the Surgical Service of the Roosevelt Hospital.

*Operation.*—A subcostal incision, with division of the left rectus and oblique muscles, was made on the left side. The gastrocolic omentum was divided and the mass exposed. It proved to be a somewhat purplish, cystic tumor about 14 cm. in diameter springing from the tail of the pancreas. After incision of the peritoneal covering, the tumor was freed down to the point of its attachment to the pancreas. The splenic vessels were isolated and retracted after division and ligation of their pancreatic branches. The tail of the pancreas was divided between clamps, and a segment 8 cm. long was removed with the attached tumor. The pancreatic stump was closed with interrupted sutures of black silk. Careful palpation of the head of the pancreas failed to reveal any nodules. The gastrocolic omentum was reconstructed. The wound was closed in layers without drainage. The time for the operation was one hour thirty-five minutes. The procedure was well borne.

*Pathologist's Report.*—The specimen measures 12 by 15 cm. in its diameter. Its surface is smooth except at the point of attachment to a mass of finely lobulated tissue which appears to be pancreas and which measures 8 by 3.6 cm. The tumor contains 450 cc. of bloody fluid in which there are large masses of apparently necrotic, friable, grayish yellow material. The cyst wall measures up to 1 cm. in thickness and is composed of soft reddish gray tissue. The lining is gray and smooth except in areas to which necrotic fragments are adherent. There is a line of cleavage between the pancreatic tissue and the cystic mass.

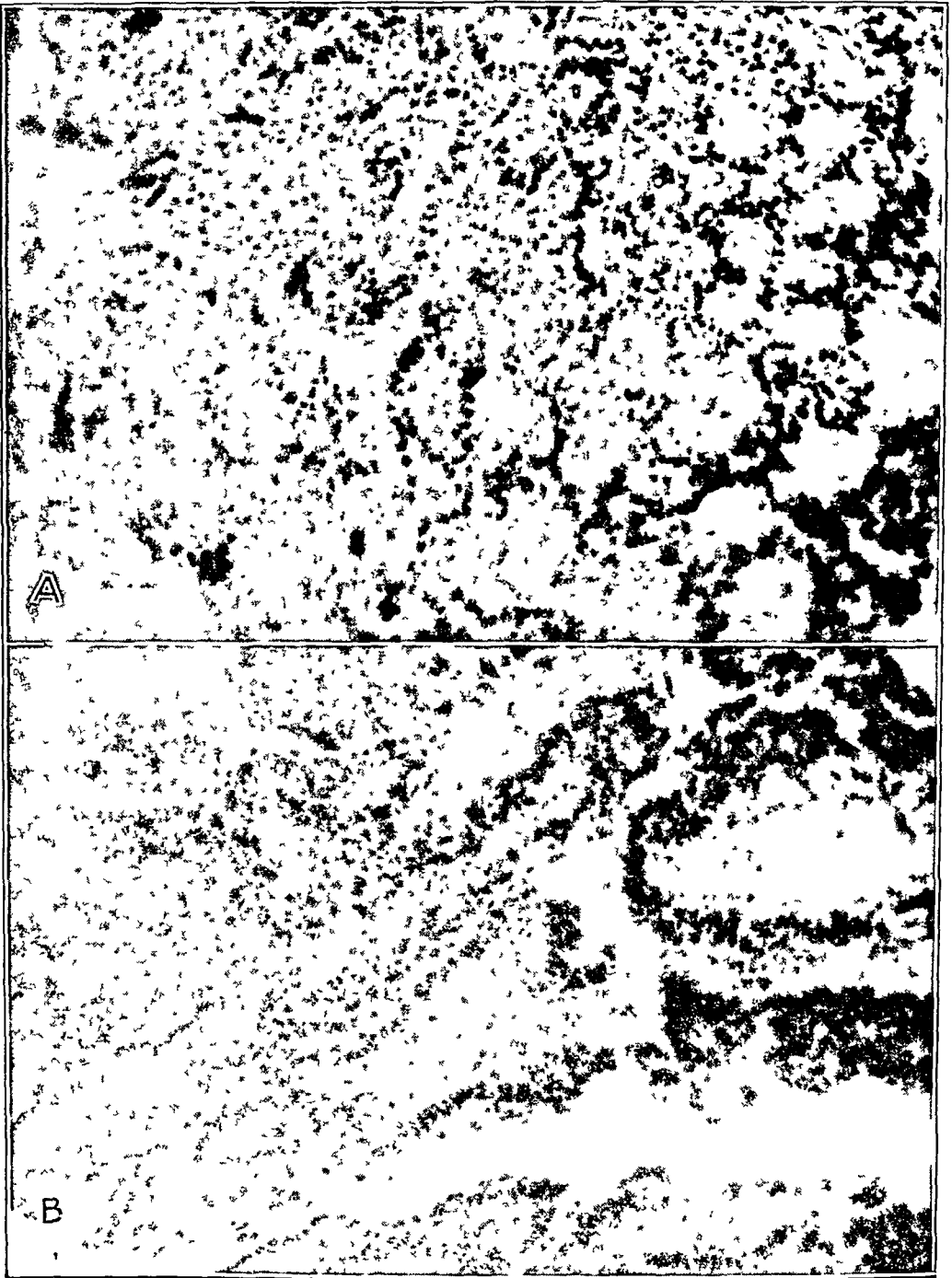
*Microscopic Examination* (figure 8).—The finely lobulated structure is the pancreas. The alveoli are not unusual, but there is some fat infiltration in the stroma. There are abundant, apparently normal islets of Langerhans. The interlobular arterioles are slightly thickened, and there is some increase in perivascular fibrous tissue. In one section of the wall of the cyst there is a wide zone of fibrous tissue. On the inner surface of this tissue there is pink-stained material which is amorphous except for slits in its substance which suggest the presence of cholesterol or fatty acids.

Within the fibrous tissue there are numerous large islands of epithelial cells. In this section there is some suggestion of papillary forms, but it is more characteristic for the cells to occur as solid, irregularly shaped sheets. The cells are small but uniform in size. They have a finely granular, pale pink cytoplasm and round or oval nuclei with moderate quantities of chromatin which is uniformly distributed throughout the nuclei in coarse granules. In other areas there is less fibrous tissue and there are more definite papillary forms. In general, however, the epithelial cells are arranged in elongated epithelial sheets. The individual cells in these areas are similar to those described. There are occasional large, hyperchromatic nuclei. Some islands of epithelium are present in vascular spaces.

*Diagnosis.*—The diagnosis was islet cell tumor of the pancreas. The slides were submitted to Dr. Virginia Kneeland Frantz and Dr. Arthur Purdy Stout. It was their opinion that we were dealing with an islet cell tumor despite the unusual gross features of the specimen. All except a single reported islet cell tumor have been solid structures. Dr. Frantz also pointed out that the criteria of malignancy in these growths are not well defined and that the epithelial tissue in the vessels did not establish the growth as malignant.

*Course.*—The patient made a smooth, uneventful recovery and was discharged from the hospital on the seventeenth postoperative day. Her wound was well healed, and she was entirely free of symptoms. On Oct. 7, 1946, four years and five months after operation, she was readmitted to the Roosevelt Hospital and an emergency operation was performed for acute perforation of a gastric ulcer.



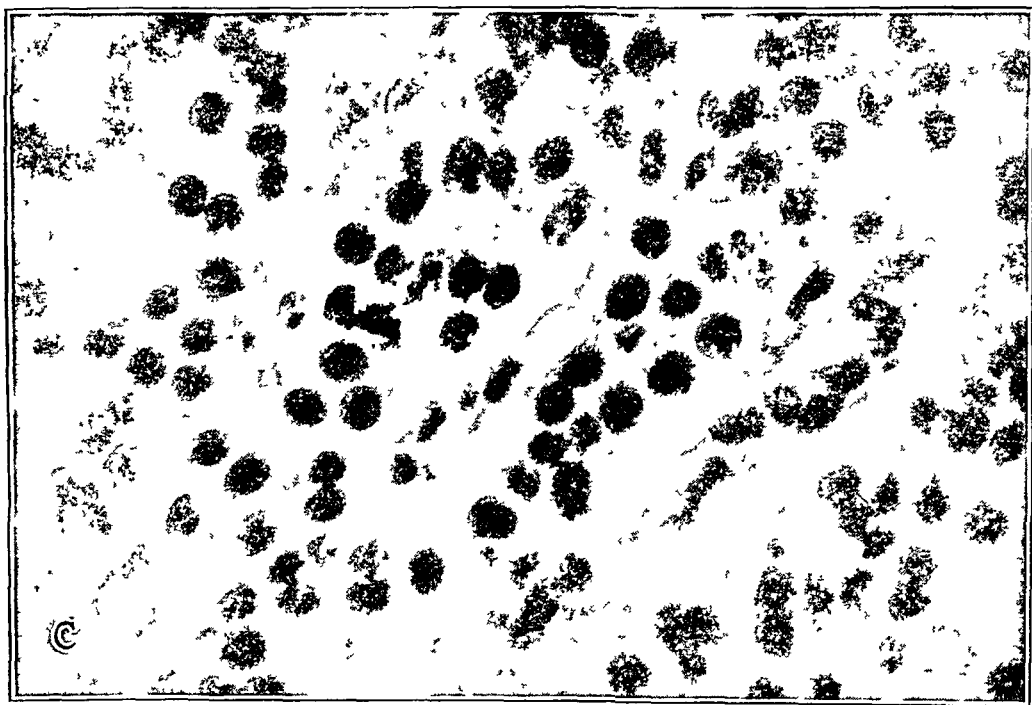


Islet cell tumor of pancreas. *A*, section through subcapsular area. Low power magnification; hematoxylin and eosin. *B*, section through inner portion of tumor. Low power magnification, hematoxylin and eosin.

A simple closure of the perforation was performed after excision of tissue from its edges for microscopic examination. Exploration of the abdomen revealed no evidence of recurrence of the tumor removed in May 1942. The patient had a smooth convalescence and when last examined was feeling well.

#### COMMENT

Numerous theories on the origin of islet cell tumors have been proposed. It may be said that, in general, there have been three basic concepts: 1. The tumors arise from embryonal rests. 2. The tumors arise from preexisting mature islands. 3. The tumors arise from the excretory ducts of the pancreas. Histologic and embryologic investi-



C, high power magnification showing sheets of islet cells with deeply-staining uniform round nuclei.

gations<sup>1</sup> have indicated that the epithelial cells of the islets are derived from the epithelium lining the small excretory ducts of the pancreas. It has long been known that after ligation of the pancreatic ducts the islet tissue persisted and the acinar cells atrophied. In the process of regeneration of the pancreas following temporary ligation, it has been demonstrated<sup>2</sup> that duct epithelium gives rise to both islet and acinar

1. Bensley, R. R.: Studies on the Pancreas of the Guinea Pig, *Am. J. Anat.* **12**:297, 1911. O'Leary, J. L., and Womack, N. A.: Histology of Adenoma of Islets of Langerhans, *Arch. Path.* **17**:291 (March) 1934.

2. Grauer, T. P.: Regeneration in the Pancreas of the Rabbit, *Am. J. Anat.* **38**:233, 1926.

tissue. In a recent publication, Good<sup>3</sup> has shown, on the basis of careful histologic investigation, that the structure of the wall of the pancreatic duct and that of the wall of the capsule of an islet tumor is the same and that, in fact, the capsule is the duct wall. He further believes that the presence or absence of a capsule depends on whether the tumor took origin in a duct with or without a wall.

The number of reported cases of islet cell tumor without hypoglycemia, exclusive of those found incidentally at autopsy, is small.<sup>4</sup> This is readily understandable since, in the absence of clinical symptoms of hypoglycemia, these tumors would be removed in all probability only if they should grow large enough to be discovered by abdominal palpation or in the event of massive malignant degeneration or perhaps unexpectedly in the course of abdominal exploration.

It is difficult to explain why certain islet cell tumors produce hypoglycemia while others do not. It is also difficult to understand why a large tumor such as that reported by Brunschwig,<sup>5</sup> measuring over 10 cm. in diameter, should not produce a more severe clinical picture than the average tumor measuring only 1 or 2 cm. in diameter. The cells of an inactive tumor, i. e., one not producing hypoglycemic symptoms, may be filled with the typical granules characteristic of the tumor which produces hyperinsulinism.<sup>6</sup>

In approximately 15 per cent of the reported cases more than one tumor was found at operation. While in most instances multiple tumors will be found within a few centimeters of each other in the tail or body of the pancreas, the frequent finding of a solitary or second tumor in the head of the organ makes thorough palpation of the entire organ imperative. However, many recorded cases indicate that even the most careful palpation may be deceptive and one or more small tumors may be overlooked.<sup>4a</sup>

#### SUMMARY

A report is made of an unusually large islet cell tumor of the pancreas which showed a rare cystic degeneration and did not produce hypoglycemic symptoms.

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3. Good, L. P.: Origin and Growth of an Adenoma of the Islands of Langerhans, *Surgery* **18**:159, 1945.

4. (a) Frantz, V. K.: Adenomatosis of Islet Cells, with Hyperinsulinism, *Ann. Surg.* **119**:824, 1944. (b) Sailer, S., and Zininger, M. M.: Massive Islet Cell Tumor of the Pancreas Without Hypoglycemia, *Surg., Gynec. & Obst.* **82**:301, 1946.

5. Brunschwig, A.: Large Islet Cell Tumor of the Pancreas, *Surgery* **9**:554, 1941.

6. Whipple, A. O.: Pancreaticoduodenectomy for Islet Carcinoma, *Ann. Surg.* **121**:847, 1945.

# GRANULOMAS OF THE ILEOCECAL REGION SECONDARY TO APPENDICITIS (LIGNEOUS CECITIS) WHICH SIMULATE NEOPLASMS

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THIS STUDY was prompted by the occasional observation of specimens of the right part of the colon in cases of lesions which had been surgically diagnosed as carcinoma of the cecum and which, on pathologic examination, turned out to be merely inflammatory reactions about a diseased appendix. It was our objective to try to establish more exact methods of recognizing this condition so that a less radical operation might be done. In this regard, it was deemed necessary to investigate, as well, cases in which only appendectomy was done, to determine whether this operation alone could bring about cure in the face of the extensive inflammatory reaction about the offending appendix.

## REVIEW OF THE LITERATURE

These lesions have been described under a number of titles in the literature. Prior to the classic paper on appendicitis by Fitz,<sup>1</sup> every kind of inflammatory lesion of the right side of the abdomen and pelvis was included under the term "typhlo-enteritis." After that time there arose a controversy as to whether any such entity as primary typhlitis existed or whether all forms of typhlitis originated in the

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Abridgment of thesis submitted by Dr. J. S. Wilson to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery.

Dr. Wilson is a fellow in surgery at the Mayo Foundation, Dr. Dockerty is from the Section on Surgical Pathology, Dr. Waugh is from the Division of Surgery and Dr. Borgen is from the Division of Medicine, Mayo Clinic.

1. Fitz, R. H.: *Perforating Inflammation of the Vermiform Appendix, With Special Reference to Its Early Diagnosis and Treatment*, Boston M. & S. J. 115: 13 (July 8) 1886.

appendix.<sup>2</sup> Concurrently with the development just described, a good deal of interest was shown in nonspecific granulomatous lesions in the abdomen which were mistaken for neoplasms.<sup>3</sup>

W. J. Mayo<sup>4</sup> was the first surgeon to make a definite reference to appendical inflammations which were indistinguishable from neoplastic disease. Bergmann<sup>21</sup> collected the largest series, namely, 15 reports of cases of cecal granulomas secondary to appendicitis.

Individual cases or small series have been reported under a variety of titles. Goto,<sup>5</sup> Låwen,<sup>6</sup> Ravdin and Rhoades<sup>7</sup> and Homans and

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2. (a) Bernard, R., and Milone, S.: Typhlites aiguës et chroniques et leurs rapports avec l'appendicite, *Arch. d. mal. de l'app. digestif*. **20**:1052-1069, 1930. (b) Biedermann, H.: Durch Darmresektion geheilte primäre Phlegmone des Dickdarms mit Inversion der Coecalwand, *Beitr. z. klin. Chir.* **124**:718-722, 1921. (c) Brams, W. A., and Meyer, K. A.: A Study of Acute, Primary Typhlitis, *J. A. M. A.* **84**:436-437 (Feb. 7) 1925. (d) Bryan, W. A.: Simple Inflammatory Lesions of the Cecum, *Tr. South. S. A.* **43**:320-330, 1930. (e) Fiolle, J.; Luccioni, F., and Luccia, H.: Les typhlites appendiculaires à retardement: Ictus cæcoux; Formes gangreneuses, formes abortives, *J. de chir.* **42**:177-189 (Aug.) 1933. (f) Lazarus, J. A.: Primary Inflammatory Tumor of the Cecum Without Appendicitis, *Am. J. Surg.* **1**:350-356 (Dec.) 1926. (g) Nemilov, A.: Ueber entzündliche Dickdarmgeschwülste und ihre Bedeutung in der Pathologie des Blinddarms, *Arch. f. klin. Chir.* **153**:346-357, 1928. ((h) Powers, J. H.: Unusual Inflammatory Lesions of the Ileocecal Region, *Ann. Surg.* **103**:279-289 (Feb.) 1936. (i) Bergmann, V., cited by Låwen.<sup>6</sup>

3. (a) Bachlechner, K.: Ueber entzündliche Ileocolcaltumoren, *Beitr. z. klin. Chir.* **124**:103-115, 1921. (b) Bargaen, J. A., and Jacobs, M. F.: Inflammatory Cecal Tumors: Diagnosis of Types of Obscure Etiology, *Arch. Surg.* **20**:832-850 (May) 1930. (c) Barnes, J. P.: Non-Specific Granuloma of the Colon, *Texas State J. Med.* **39**:529-532 (Feb.) 1944. (d) Braun, H.: Ueber entzündliche Geschwülste am Darm, *Deutsche Ztschr. f. Chir.* **100**:1-12, 1909. (e) Korte, W.: Ueber entzündliche Geschwülste am Darm, *Arch. f. klin. Chir.* **118**:138-163, 1921. (f) Mock, H. E.: Infective Granuloma: Non-Specific Chronic Tumor-Like Productive Inflammations of Gastro-Intestinal Tract, *Surg., Gynec. & Obst.* **52**:672-689 (March) 1931. (g) Moynihan, B. G. A.: The Mimicry of Malignant Disease in the Large Intestine, *Edinburgh M. J.* **21**:228-236 (Jan.) 1907. (h) Moschcowitz, E., and Wilensky, A. O.: Non-Specific Granulomata of the Intestine, *Am. J. M. Sc.* **166**:48-66, 1923. (i) Rankin, F. W.; Bargaen, J. A., and Buie, L. A.: The Colon, Rectum, and Anus, Philadelphia, W. B. Saunders Company, 1932, p. 203. (j) Robson Mayo, A. W.: Some Abdominal Tumors Simulating Malignant Disease and Their Treatment, *Brit. M. J.* **1**:425-428 (Feb. 22) 1908. (k) Virchow, R., cited by Teitze.<sup>17b</sup>

4. Mayo, W. J.: Inflammations Involving the Caecum: Its Appendix or Both, *Tr. Minnesota M. Soc.*, 1888, pp. 63-72.

5. Goto, S.: Ueber die einfache chronische entzündliche Strictur des Darmes, *Arch. f. klin. Chir.* **97**:190-206, 1912.

6. Låwen, A.: Ueber Appendicitis fibroplastica, *Deutsche Ztschr. f. Chir.* **129**:221-241, 1914.

7. Ravdin, I. S., and Rhoades, J. E.: Regional Ileitis and Fibroplastic Appendicitis, *Ann. Surg.* **106**:394-404 (Sept.) 1937.

Hass<sup>8</sup> wrote about fibroplastic appendicitis. Moschcowitz and Wilensky<sup>3h</sup> used the term "nonspecific granuloma," and Mock<sup>3t</sup> presented a great deal of pathologic substantiation for the use of the name "infectious granuloma." Kelly and Hurdon<sup>9</sup> wrote about circumscribed appendical abscesses, while Walters and Synhorst<sup>10</sup> and Caylor<sup>11</sup> used the term "ligneous inflammation of the cecum." Many of the cases in the aforementioned papers do not conform to the rigid criteria used in selecting the cases for this study.

Since the establishment of regional enteritis as an entity,<sup>12</sup> there has been some controversy as to whether appendical granulomas are not unusual manifestations of this disease.

#### INCIDENCE

These lesions are rare. Bachlechner<sup>3a</sup> collected reports of 41 cases but did not give a detailed summary of those he included. Bernard and Milone<sup>2a</sup> were able to add 20 cases, while Ravdin and Rhoades a few years later found reports of only 15 cases after the time of the appearance of Bachlechner's paper.

#### ETIOLOGY AND PATHOGENESIS

Perforation of the appendix as the initiating lesion in these tumors was noted by numerous authors.<sup>13</sup> In other cases the lesion was ascribed to prolonged, mild inflammation about appendical fecaliths and foreign bodies.<sup>14</sup> Prolonged low grade infection without obstructive features was incriminated by some writers and usually was associated with a large thickened appendix.<sup>15</sup> Two cases were reported

8. Homans, J., and Hass, G. M.: Regional Ileitis: A Clinical, Not a Pathological Entity, *New England J. Med.* **209**:1315-1324 (Dec. 28) 1933.

9. Kelly, H. A., and Hurdon, E.: *The Vermiform Appendix and Its Diseases*, Philadelphia, W. B. Saunders and Company, 1905, p. 321.

10. Walters, W., and Synhorst, A. P.: Ligneous Infection of the Cecum Resulting from Subacute Appendicitis, *S. Clin. North America* **6**:1203-1206 (Oct.) 1926.

11. Caylor, H. D.: Cecum lignum, *J. Indiana M. A.* **31**:62-65 (Feb.) 1938.

12. Barbosa, J. deC.; Bagen, J. A., and Dixon, C. F.: Regional Segmental Colitis, *S. Clin. North America* **25**:939-968 (Aug.) 1945. Crohn, B. B.; Ginzburg, L., and Oppenheimer, G. D.: Regional Enteritis: A Pathological and Clinical Entity, *J. A. M. A.* **99**:1323-1329 (Oct. 15) 1932.

13. Hartwell, J. A.: Non-Tuberculous Inflammation of the Cecum, *S. Clin. North America* **1**:361-365 (April) 1921. Okinckzyk, cited by Bernard and Milone.<sup>2a</sup> Rhoades, R. L.: Discussion, *Tr. South. S. A.* **43**:329-330, 1930. Bernard and Milone.<sup>2a</sup> Bachlechner.<sup>3a</sup> Korte.<sup>3e</sup> Walters and Synhorst.<sup>10</sup>

14. Bernard and Milone.<sup>2a</sup> Bachlechner.<sup>3a</sup> Låwen.<sup>6</sup> Korte.<sup>3e</sup> Kelly and Hurdon.<sup>9</sup>

15. (a) Gangitano, F.: Ueber periappendiculäre pseudo-neoplastische entzündliche Tumoren, *Arch. f. klin. Chir.* **89**:399-422, 1909. (b) Kolouch, F. G.: Non-Tuberculous Inflammation of the Cecum: Report of Case, *Nebraska M. J.* **8**:106-107 (March) 1923. (c) Bernard and Milone.<sup>2a</sup> (d) Bryan.<sup>2d</sup> (e) Bachlechner.<sup>3a</sup> (f) Ravdin and Rhoades.<sup>7</sup>

in which the lesion arose in the residual stump of an incompletely removed appendix.<sup>16</sup> Several authors<sup>17</sup> cited cases in which the lesion arose around nonabsorbable suture material used during appendectomy. Nemilov<sup>2g</sup> particularly expressed a belief that there was a real danger of intramural abscess formation when nonabsorbable material was used for both the appendical stump ligature and the purse-string suture since this procedure resulted in trapping infected mucosa between the suture lines.

Mock<sup>3f</sup> and Gangitano<sup>15a</sup> each reported a case in which trauma played a part in initiating granulomatous lesions.

Bernard and Milone were the only authors to point out that in the patients involved the appendix was frequently retrocecal and that the average age was over 40 years. They expressed the thought that this combination of an appendix with a lowered secretory function lying in an easily walled-off space accounted for the chronic, localized inflammatory reaction.

The extension of the inflammation to the ileum and cecum was explained on the basis of contiguity by most authors. Some of the French writers<sup>18</sup> expressed a belief that retrograde arterial thrombosis and thrombosis of the ileocecal veins were factors in the spread of the process. Mock expressed a belief that the underlying cause was a local interference with the blood supply. He postulated a vicious circle of inflammatory vascular occlusion, focal necrosis and reactive fibrosis which caused obliteration of more vessels and consequent slow progression of the necrotizing process. Låwen suggested that the fibrous overgrowth was due to a fibroplastic diathesis but offered no supportive evidence for this view.

#### PATHOLOGIC PROCESS

The gross picture as described in the literature was that of a fibrous mass sometimes containing small abscesses. As Mock pointed out, the tumor at times was the size of a grapefruit, irregular in outline, and included adjacent tissues within its boundaries. The consistency varied from hard induration to soft abscess cavities, and the neighboring lymph nodes were frequently enlarged.

Microscopically, the prominent feature was the marked increase in fibrous tissue, which varied from dense scar to young granulation tissue. Interspersed throughout this tissue were areas of round cell

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16. Bernard and Milone.<sup>2a</sup> Nemilov.<sup>2g</sup>

17. (a) Routier, cited by Gangitano.<sup>15a</sup> (b) Tietze, A.: Ueber entzündliche Dickdarmgeschwülste, *Ergebn. d. Chir. u. Orthop.* **12**:211-273, 1920. (c) Mock.<sup>3f</sup>

18. Hovelacque, and Sourdin, cited by Bernard and Milone.<sup>2a</sup> Bernard and Milone.<sup>2a</sup> Fiolle, Luccioni and Luccia.<sup>2e</sup>

infiltration, microscopic abscesses filled with polymorphonuclear leukocytes, areas of necrosis and scattered giant cells. Låwen and Mock noted the frequency of occurrence of occlusive thickening of the media of the arterioles.

#### DIAGNOSIS

As a rule the clinical diagnosis was carcinoma, though Barga and Jacobs<sup>3b</sup> threw some light on the diagnosis of these lesions by pointing out that a sense of well-being, absence of anemia and lack of the typical roentgenologic<sup>19</sup> picture of carcinoma would help in distinguishing granulomatous from malignant lesions.

The surgical diagnosis was frequently faulty, and in 1 of Mock's cases even the employment of frozen sections did not result in the making of a correct diagnosis. The only aid suggested was a statement by Bernard and Milone that in cases of these lesions there is a line of cleavage behind the cecum which leads to the diseased appendix.

#### TREATMENT

In 4 cases appendectomy<sup>20</sup> and in 1 coring out of the appendical mucosa<sup>10</sup> resulted in cure. Ileocolostomy was successful in several instances, while in other cases<sup>21</sup> it failed and resection was necessary. Most of the tumors were resected as carcinoma. All patients who survived did well, but in some chronic sinuses developed, and a few patients died of peritonitis.

#### SELECTION OF CASES

In order to obtain the material for this study, the surgical files of the Mayo Clinic were searched for records bearing the diagnosis of "inflammatory lesion of the right side of the colon," "perityphlitis," "appendical or periappendical granuloma" and similar conditions. The period covered was the years 1905 to 1945 inclusive. Discarded were cases in which inadequate material was available for pathologic study. Also eliminated were all cases in which regional enteritis and segmental ulcerative colitis might be present. In the first place all case records were checked for later development of recurrence of symptoms or of clinical or roentgenologic evidence suggesting regional enteritis or colitis.<sup>22</sup> As a further safeguard, no case was included in which there was even microscopic evidence of ulceration of the mucosa of the ileum

19. Weber, H. M.: Non-Neoplastic Tumefactive Lesions of the Large Intestine: Inflammatory Tumefactions, *Am. J. Roentgenol.*, **36**:637-647 (Nov.) 1935.

20. Caylor.<sup>11</sup> Gangitano.<sup>15a</sup>

21. Nemilov.<sup>28</sup> Låwen.<sup>6</sup>

22. Hadfield, G.: The Primary Histological Lesion of Regional Ileitis, *Lancet* **2**:773-775 (Oct. 7) 1939. Barga and Jacobs.<sup>3b</sup>



or colon. In addition, all specimens showing inflammatory changes in the wall of the ileum or colon beyond the immediate confines of the granuloma were rejected.

It was felt that the employment of these rigid criteria should adequately rule out regional enteritis in all cases in which hemicolectomy was done on the right side. In cases in which only the appendix was removed there could be some doubt. In the last-mentioned cases, however, there were definite serious pathologic changes in the appendixes, and the surgical notes on the records indicated that the ileum and colon were grossly normal.

In order to be sure that the lesions associated with appendical disease were typical granulomas, certain arbitrary rules were established. No cases were included in which a fistula or sinus persisted after drainage of an appendical abscess, as it was felt that the drainage could be held responsible for the excessive response of the fibrous tissue. Whenever a frank appendical abscess of moderate size was found, even though it was encapsulated and mistaken for carcinoma, the case was rejected. Furthermore, when the mass was resected and found to consist only of dense fibrous adhesions, the case was not included even though a previous ileocolostomy had been done which had resulted in considerable diminution of the size of the tumor. Such a response might well indicate resolution of a granulomatous process, but, since the assumption could not be proved, the cases were eliminated.

Needless to say, in none of the group used was there evidence clinically, surgically, pathologically, bacteriologically or on follow-up of syphilis, actinomycosis, tuberculosis, amebiasis or lymphogranuloma. In one instance the possibility of a healed ruptured diverticulum could not be excluded and the case was rejected.

#### METHODS OF STUDY

Pathologic material, available in all cases, had been preserved in 10 per cent solution of formaldehyde. This material was secured and studied in great detail. Sections were taken from the granulomatous mass, from the appendix if present and from the ileal and cecal walls and the lymph nodes. In some cases large mounted microscopic sections were made through the whole tumor to study its over-all structure.

#### REPORT OF ILLUSTRATIVE CASES

Twenty cases were used for study, and almost as many probable cases were excluded for the reasons mentioned previously. In all these the lesion was mistaken for a malignant one by either the clinician, the roentgenologist or the surgeon and sometimes by all three (table 1). Four of these cases will be reported in detail to illustrate some of the

TABLE 1.—*Summary of Diagnoses, Treatment and End Results*

Case	Diagnosis			Treatment	
	Clinical	Roentgenologic	Surgeon's	Type	End Result
1	Carcinoma 90 per cent; inflammatory 10 per cent; probably carcinoma	Filling defect of cecum; intrinsic or extrinsic	Inflammatory mass but might be carcinoma or actinomycosis	One stage resection	Well 6 yr. later
2	Diverticulitis (?) or appendicitis	Filling defect of the right transverse and hepatic colon	Carcinoma	One stage resection	Died fifth post-operative day
3	Cecal tumor, probably malignant	Cecal deformity	First stage: carcinoma; second stage: stricture from abscess	Two stage resection	Well 13 yr. later
4	Cecal carcinoma, appendiceal abscess (?)	Indeterminate lesion, right part of colon	First and second stages: carcinoma	Two stage resection	Recovered from operation
5	Cecal carcinoma	Cecal carcinoma	Cecal carcinoma	One stage resection	Well with normal bowel on roentgen ray study 1 yr. later
6	Cecal mass, possibly malignant	Operable lesion involving terminal part of ileum and possibly cecum	Cecal mass, malignant (?)	Two stage resection	Well 6 yr. later
7	Cecal carcinoma	Carcinoma of tip of cecum or appendix	Perforating carcinoma, head of cecum	Exteriorized	Well with normal bowel on roentgen ray study 4 yr. later
8	Subacute appendicitis, abscess (?)	No roentgenogram of colon	Cecal carcinoma	Exteriorized	Well 2 yr. later
9	Granuloma of appendix stump, carcinoma (?), regional enteritis (?)	Deforming lesion of cecum	Cecal carcinoma	One stage resection	Well 2 yr. later
10	Cholecystitis, cholelithiasis	Nonfunctioning gallbladder; no roentgenogram of colon	Cecal mass, malignant (?); cholelithiasis	One stage resection	Well 5 yr. later
11	Cholecystitis, appendicitis	Normally functioning gallbladder; no roentgenogram of colon	Ileocecal mass, suggestive of carcinoma	One stage resection	Repeated drainage and abscess formation from fistula; no evidence of regional enteritis by roentgen ray 7 yr. later
12	Cecal tumor, appendicitis (?)	Cecal lesion (?)	Ligneous cecal infection	Appendectomy	No known recurrence of bowel trouble at death 7 yr. later
13	Cecal tumor, appendiceal abscess (?)	Roentgenogram of colon unsatisfactory	Old chronic suppurating appendicitis	Appendectomy	Good recovery from operation
14	Abdominal tumor; exploration elsewhere, diagnosed retroperitoneal lipoma	Indefinite mass extrinsic to right part of colon	Granuloma from old perforated appendix	Appendectomy	Well 11 yr. later; small bowel obstruction from adhesions 10 yr. after operation
15	Cecal carcinoma, appendiceal granuloma (?)	Obstructing cecal lesion, probably carcinoma	First stage: cecal carcinoma; second stage: granuloma from old perforated appendix	Ileocolostomy, appendectomy	Well 1 yr. later
16	Obstructing carcinoma, right part of colon	Distortion of right part of colon, nature lesion indeterminate	Granuloma from old perforated appendix	Appendectomy	Well 3 yr. later
17	Cecal carcinoma	Cecal carcinoma	Probably inflammatory tumor	One stage resection	Died seventh post-operative day
18	Elsewhere: cecal carcinoma; at clinic: recurrent appendicitis	Colon normal	Inflammatory tumor, terminal part of ileum and cecum	One stage resection	Well 5 yr. later
19	Cecal tumor, tuberculosis (?)	Filling defect of cecum and sigmoid	Inflammatory mass attached to abdominal wall and sigmoid	One stage resection	Roentgenogram of colon normal 19 yr. later
20	Cecal mass (?), inflammatory; tuberculosis (?)	Blind loop of bowel in cecal area	Mass of adhesions, enlarged nodes; no definite tumor	Two stage resection	Well 14 yr. later

difficulties experienced in the diagnosis of this disease. The case numbers are those used in tables 1, 2 and 3.

CASE 2.—A 69 year old man was admitted to the hospital in a state of subacute illness of four months' duration with a history of intermittent pain in the left upper abdominal region varying from sharp to dull in intensity. His attacks lasted as long as a week and were not related to effort or intake of food. The intake of sodium bicarbonate and food did not relieve them. For one week preceding his admission the pain had shifted to the right middle and lower portions of the abdomen and had become more severe, especially at night. There was no vomiting, constipation or diarrhea, but he had noted anorexia for several months and mild nausea for a week. The patient himself had detected a mass in the right side of the abdomen five days previously. Physical examination disclosed a tender mass in the right flank extending from the brim of the pelvis to a point above the umbilicus. He had considerable arteriosclerosis, and his pulse showed frequent extrasystoles. The value for hemoglobin was 78 per cent, the erythrocyte count was 4,290,000 per cubic millimeter of blood and the leukocytes numbered 12,400. There was albuminuria, grade 1, and pyuria, grade 1 (on a basis of 1 to 4, with 1 representing the least and 4 the most severe condition). Roentgenologic studies of the colon made with the aid of barium sulfate showed a filling defect in the hepatic and transverse portions.

The abdomen was explored after a diagnosis of perforating carcinoma of the ascending colon or possibly diverticulitis had been made. A large mass, which surrounded the cecum and ascending colon and which the surgeon considered malignant, was resected.

The patient's postoperative course was extremely stormy, and cardiac and respiratory failure developed. He died on the fifth postoperative day. Post-mortem examination revealed generalized peritonitis.

On surgical pathologic examination the specimen was found to consist of 20 cm. of ileum, the appendix, cecum, ascending colon and 8 cm. of transverse colon (fig. 1). In the center of the tumor a twisted, retrocecal and retroileal appendix was found. In the midportion of the appendix there was a small perforation leading to an abscess 3.0 by 1.5 by 1.0 cm. which lay between the appendix and the adherent cecum.

On microscopic examination sections of the appendix at the site of rupture showed absence of the mucosa and the presence of dense infiltration with lymphocytes, monocytes and a few scattered polymorphonuclear leukocytes. This reaction involved all coats of the appendix and was interspersed with a dense proliferation of fibroblasts which almost replaced the muscularis propria. The fibrosis extended into the fat of the mesoappendix. The walls of the abscess cavity and the overlying cecum revealed a dense infiltration with polymorphonuclear leukocytes, monocytes, lymphocytes and occasional plasma cells. In some areas fibroplastic activity was intense. The adherent mesentery was involved by a similar acute and subacute inflammatory process, largely perivascular in distribution and characterized by the presence of dense bands of fibrotic tissue.

The preceding case illustrates a relatively insidious onset and an atypical location of the pain early in the process, with the subsequent development of a huge tumor which became evident to the patient himself. It also illustrates the danger of primary one stage resection as a means of surgical relief.

CASE 9.—Fourteen months before her admission to the hospital a young woman, aged 21, after feeling run down for several months and losing 20 pounds (9.1 Kg.), began to have abdominal cramps and pain in the right lower quadrant. At operation elsewhere a gangrenous appendix was removed. The convalescence was normal. She remained well until three weeks before her admission, when she noted vague distress in the lower abdominal region and ten days later detected a tender mass in the right lower quadrant, which increased in size slightly. A week before her admission she began to have severe pain in the right lower quadrant, which was relieved by vomiting. At the same time her temperature rose to 99.0 F.

Physical examination revealed a well developed young woman with a movable, tender, tympanitic mass, 6 cm. in diameter, under a healed scar at McBurney's point.

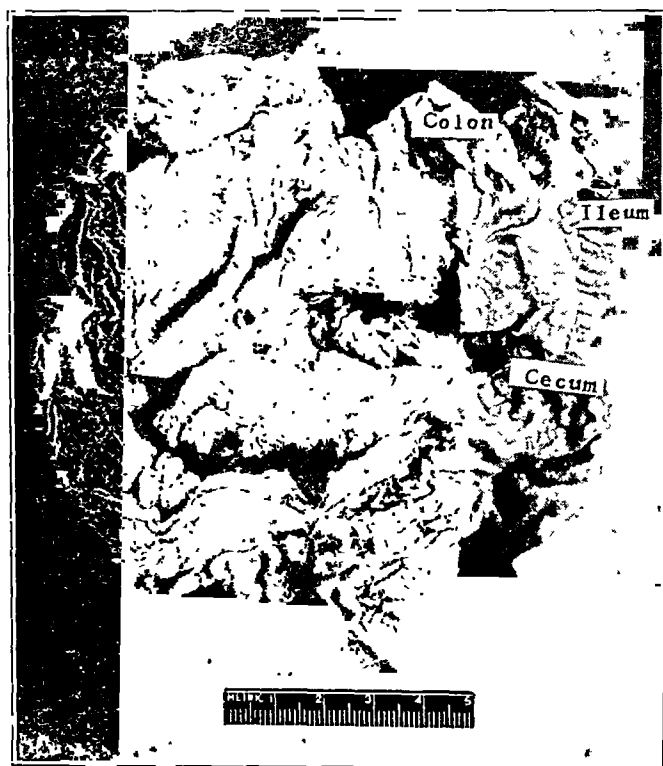


Fig. 1 (case 2).—Granuloma opened to show overgrowth of dense fibrous tissue. Note the white probe in the perforation of the appendix.

The hemoglobin measured 12.1 Gm. per hundred cubic centimeters of blood, the erythrocytes numbered 3,980,000 and the leukocytes count was 6,900 per cubic millimeter of blood. The urine was normal. Roentgenologic studies disclosed a deforming lesion of the cecum.

The diagnoses of granuloma of the appendical stump, neoplasm and regional enteritis were considered, and exploration was carried out. The surgeon found a mass associated with considerable glandular involvement; he thought the lesion was a carcinoma and carried out a primary resection.

The patient made a good recovery and was well two years later.

The gross pathologic specimen consisted of 13 cm. of the terminal part of the ileum and 14 cm. of cecum and ascending colon. The base of the cecum and the terminal part of the ileum were adherent to a glandular tumor mass 5 by 5 cm. lying posteromedially to the ileocecal junction. In the center of the mass was an abscess cavity 2 by 2 by 1 cm. surrounding a heavy linen ligature and a small silk suture. The linen suture had been tied in a double loop and the ends measured 1.5 cm. in length. Undoubtedly these were the materials used to tie off the stump of the appendix at the time of the previous operation.

Microscopic examination of the wall of the overlying cecum disclosed some increase in lymphocytic tissue, with a few plasma cells and polymorphonuclear leukocytes in the mucosa. The submucosa and muscularis were greatly thickened and densely infiltrated with eosinophils, plasma cells, lymphocytes and fibroblasts. The lymphocytes formed germinal follicles, and an occasional foreign body giant cell was present.

Sections from the abscess showed the center to be formed largely of polymorphonuclear leukocytes and necrotic debris, while the walls were formed of dense fibroblastic tissue which contained a few polymorphonuclear leukocytes and many lymphocytes.

The foregoing case illustrates how mild may be the symptoms of these lesions, since undoubtedly the pathologic process began soon after appendectomy and was likely due to the presence of nonabsorbable ligatures used in excessive amounts, although no symptoms appeared for over thirteen months.

CASE 15.—A 77 year old surgeon had noted a mass 1 to 2 inches (2.5 to 5 cm.) in diameter occurring in the right lower quadrant off and on for three years. It was sometimes tender, and he had occasional twinges of pain in this region. Six months before his admission to the hospital one of these attacks lasted longer than usual. At surgical exploration elsewhere a perforated appendix with abscess was found, and the latter was drained. Periodic drainage of the wound followed, and the mass remained.

Physical examination at the clinic revealed a well nourished man in apparent good health. There was a small sinus in the old appendectomy scar, and underneath it there was a smooth mass the size of an orange.

The hemoglobin measured 14.8 Gm. per hundred cubic centimeters of blood, the leukocyte count was 11,400 per cubic millimeter of blood and the sedimentation rate was 54 mm. in one hour. The urine was normal. Roentgenologic studies of the colon revealed a malignant-appearing lesion, probably carcinoma, which was obstructing and deforming the cecum.

The clinical diagnosis was probable carcinoma of the cecum, with the possibility of granuloma of the appendix being considered.

Surgical exploration revealed, in the neighborhood of the cecum, an orange-sized mass which had perforated laterally. Dissection was difficult, and since there were adherent loops of the terminal part of the ileum an ileotransverse colostomy was done. Recovery was rapid, and reexploration was carried out a month later for removal of the growth. The mass had decreased in size in the interval, and a thickened fibrotic appendix could be felt behind the cecum. The appendix was found to have ruptured at the tip and to have become fixed to the abdominal wall at the site of original drainage. Removal was accomplished. The patient was well when he was last heard from, a year later.

The appendix and its mesoappendix measured 4 by 2 by 1 cm. The mucosa contained a few polymorphonuclear leukocytes and many lymphocytes, with an increase in toxic lymph follicles. The lumen contained purulent material. The walls were the site of microscopic abscesses about which there was a dense fibroplastic reaction as well as diffuse infiltration with monocytes and lymphocytes. This process extended into the mesoappendix. In the distal portion a false diverticulum was present at the site of previous perforation. This part was the site of diffuse subacute and chronic inflammation.

The preceding case illustrates the degree to which these tumors may shrink when a shunting procedure is done. In this instance the surgeon was able to identify the appendix as the cause of the trouble and to effect cure by performing appendectomy a month after ileocolostomy had been done.

CASE 17.—A 55 year old Jewish man came for examination solely because he had found a mass in the right lower quadrant one week previously. He denied having any pain in this region but did admit having a sense of discomfort in the lower abdominal region.

Physical examination revealed arteriosclerosis and a nontender mass the size of an orange in the right lower quadrant.

The value for hemoglobin was 76 per cent, the erythrocytes numbered 4,290,000 per cubic millimeter of blood and the leukocytes 9,200. The urine contained albumin, grade 1, and pus cells, grade 1. The roentgenogram of the colon was reported as showing a defect in the terminal part of the ileum and the cecum, interpreted as being "95 per cent malignant."

The clinician agreed with the roentgenologic diagnosis, and the surgeon found a large tumor which he thought to be inflammatory. Resection was accomplished without breaking into pus. The patient did poorly after operation and died of peritonitis on the seventh day postoperatively.

The specimen removed at operation consisted of 6 cm. of the terminal part of the ileum and 11 cm. of cecum, appendix and ascending colon. The appendix was coiled up to the left of the cecum, lying between the latter and the ileum. Surrounding the appendix was a hard mass of granulation tissue 5 by 4.5 by 4 cm. which filled the interval between the ileum and cecum and extended behind the cecum. In the center of the appendix was a small perforation leading to an abscess 3 cm. (fig. 2a) in diameter which lay against the cecum.

On microscopic examination a section through the mass near the abscess showed that the mucosa of the appendix was represented by a single layer of flattened columnar epithelium and a few remnants of glands (fig. 2b). These lay along one side of the abscess, and the remainder of the appendix was replaced by microscopic abscesses and fibrous tissue, leaving only a few separated fibers of the muscularis. The abscesses were filled with polymorphonuclear leukocytes and were surrounded by dense fibrous tissue which contained foci of polymorphonuclear leukocytes and monocytes. There was remarkably little vascularization of the granulation tissue, and many of the arteries were almost obliterated by thickening of the media and, to a lesser extent, by intimal swelling.

In the adjacent cecum replacement of the subserosa and muscularis by inflammatory granulation tissue had occurred, with edema and fibrin deposits being present in the submucosa. There was some increase in number of lymph follicles in the submucosa and mucosa.

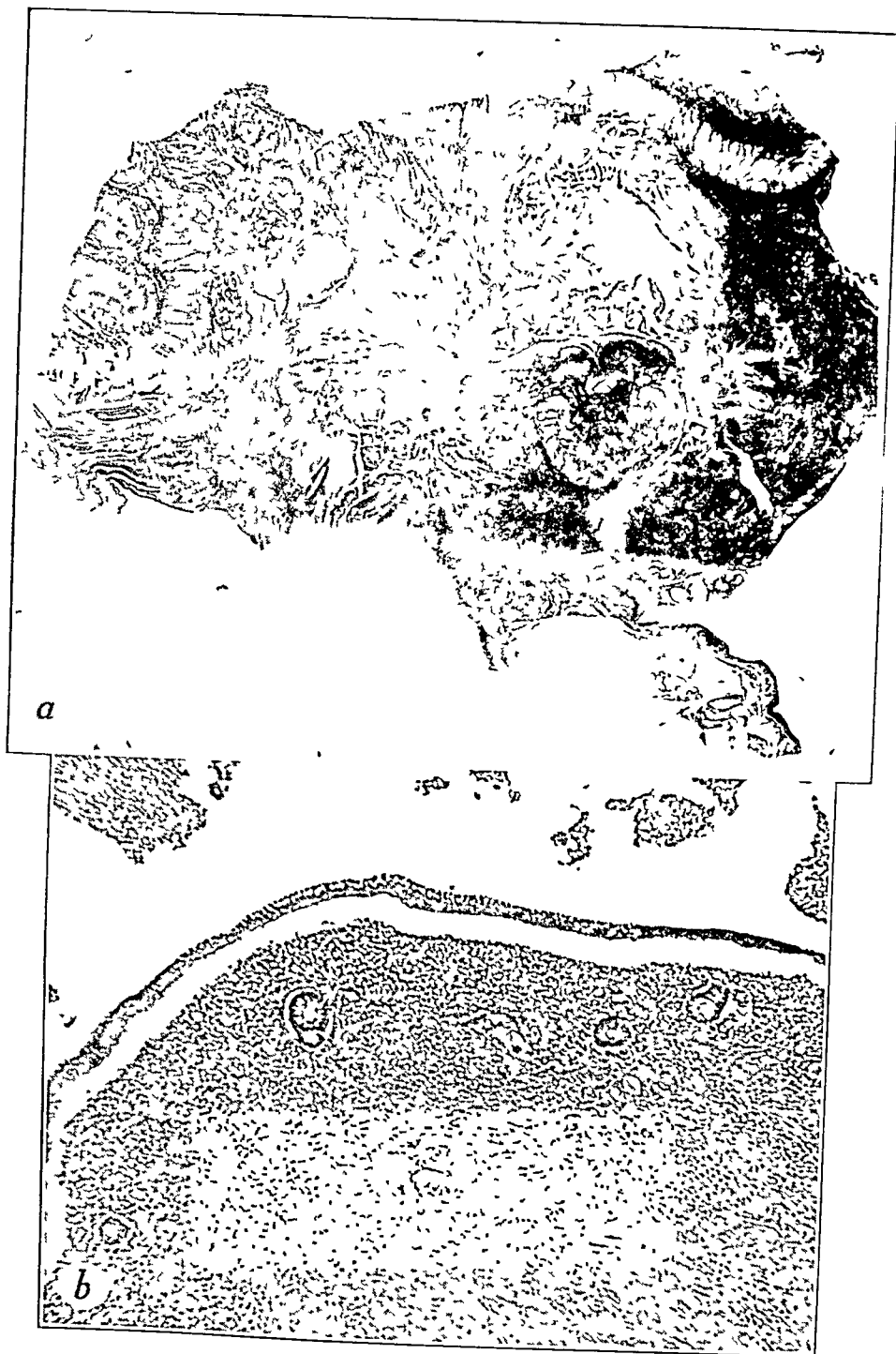


Fig 2 (case 17) — (a) Large section through the granuloma. In the appendix in the lower right hand corner there is a perforation leading to the multiloculated abscess which is surrounded by dense fibrous tissue. Note the almost normal ileal mucosa on the left. This patient had no symptoms in spite of the size of the tumor and amount of inflammation in it ( $\times 2$ ). (b) Section through the wall of the appendix near the perforation. There is marked atrophy of the mucosa, with dense infiltration of the submucosa by polymorphonuclear leukocytes (hematoxylin and eosin,  $\times 45$ ).

The preceding case is interesting because of the almost complete absence of symptoms in spite of the presence of a highly inflammatory lesion, the removal of which ended in fatal peritonitis. The danger of primary radical surgical removal of these lesions is further emphasized.

#### FINDINGS IN THE TWENTY CASES IN THIS STUDY

*Incidence.*—These lesions are rare, occurring in approximately 1 in 75,000 patients admitted to the Mayo Clinic.

*Age and Sex.*—The average age was 52.1 years, and if cases are excluded in which previous operation was partly responsible for the pathologic process, the average age was 54.8 years. There was no significant sex predilection.

*Etiology and Pathogenesis.*—Perforation: The majority of these tumors arose on the basis of perforative disease of the appendix. In 10 cases there was definite evidence of perforation, in 3 perforation was probable, in 1 there was gangrene of the tip and in 3 there were only varying degrees of inflammation (table 2).

The 5 cases in which only the appendix was removed are interesting in this regard. In these there was evidence of healed perforation along the mesenteric border at the site of entrance of the appendical vessels (fig. 3a). These could be identified grossly by the finding of slitlike breaks in what appeared to be normal muscularis. Microscopically, the mucosa did not pouch out, but the inflammatory process in the submucosa streamed through the relatively intact muscularis at these points. It would appear that as a result of a slow dilation of the lumen a pseudodiverticulum had formed and ruptured at these weak points in the muscularis. Later the mucosa had retracted and healed. The anatomic basis for this hypothesis has been well illustrated by Kelly and Hurdon<sup>23</sup> in a photograph which demonstrates the outpouchings of the mucosa at the point of the vessel attachments after enucleation of the mucous membrane. In these cases the main mass was in the appendix and its mesentery, so that it could be identified and removed. These differences in the site of perforation may be the pathologic basis for Låwen's classification of the lesions under fibroplastic appendicitis in the narrower and wider sense. That the appendixes showed no external evidence of perforation supports Chauvenet's<sup>24</sup> observation of complete macroscopic healing of a perforation in ten days.

23. Kelly and Hurdon,<sup>9</sup> p. 142.

24. Chauvenet, cited by Bernard and Milone.<sup>2a</sup>



Location of Appendix: The fact that the acute inflammatory changes could occur with such meager symptoms was largely due to the anatomic position of the appendixes (table 2).

In 13 of the 15 cases in which the site of the appendix could be determined it was retrocecal, retroileal or curled up in the ileocecal angle. In 1 patient the appendix was buried in the lateral cecal wall,

TABLE 2.—*Summary of Pathologic Findings*

Case	Size of Lesion, Cm.	Appendix		Ab- scesses *
		Position	Perforation	
1	9 by 7 by 6	Retrocecal, retroileal	Probable old perforation	3
2	12 by 7 by 6	Retrocecal, retroileal	Definite perforation	3
3	2 by 1.5 by 1.5	Retrocecal, only stump identified	Distal portion sloughed off	0
4	6 by 2 by 1.5	Retroileal	Gangrenous tips, no perforation	0
5	4 by 3.5 by 1.5	Retroileal	Old perforation	0
6	2 by 2 by 2	Ileocecal angle	Probable old perforation	0
7	6 by 4.5 by 4	Ileocecal angle	None	2
8	7 by 6 by 6	Ileocecal angle	None	0
9	5 by 5 by 5	Not present	Previously nonperforated gan- grenous appendix	3
10	5 by 5 by 4	Retroileal	Old perforation	2
11	8 by 7 by 6	Retrocecal, retroileal	Old perforation	3
12	Not stated, mass of in- durated tissue	Not stated	Old healed perforation into meso- appendix	?
13	Not stated	Lateral to cecum	Old healed perforation into meso- appendix	3
14	Not stated	Not stated	Old healed perforation into meso- appendix	2
15	Small orange	Retrocecal	Old healed perforation; false perforation	2
16	4 by 4 by 4	Buried in base of cecum	Old perforation into mesoap- pendix	1
17	5 by 4.5 by 4	Ileocecal angle	Probable old perforation; walls replaced by fibrosis and abscesses	4
18	3.5 by 3 by 3	Ileocecal angle	None	1
19	9 by 5 by 2.5	Not present	Previous rupture and partial removal	3
20	2 by 1.5 by 1	Not present	No previous perforation; partial removal	1

\* Graded from 1 to 4, in which 1 denotes the least severe and 4 the most severe condition.

and it is interesting that after a prolonged complaint of dull pain in the right lower quadrant there developed pain in the right hip which was aggravated by walking. This was probably due to extension of the process to the iliopsoas muscle. In the remaining case the appendix was buried in the base of the cecum. Thus, in all these 15 patients, the appendix was so situated that as long as the inflammatory process remained localized, which was readily accomplished by a sealing off

of the pocket in which it lay, only visceral sensation would be stimulated.

Relation of Age to Occurrence of Lesion: The tendency for these lesions to remain localized and not to go on to frank abscess formation



Fig. 3.—(a) Section through old healed perforation into the mesoappendix at the site of entry of the blood vessels. Note the almost normal muscularis at the top and bottom on the right. The mucosa on the left has healed, leaving inflammatory tissue in the submucosa; this tissue extends out into the mesoappendix along the vessels through the defect in the muscularis (hematoxylin and eosin,  $\times 25$ ). (b) Section through arterioles in the granuloma. Note increase of hyaline fibrous tissue in the media and almost complete occlusion of the lumen as a result of this increase of fibrous tissue and endothelial thickening (hematoxylin and eosin,  $\times 115$ ).

may well be related to age. Dennis and his co-workers<sup>25</sup> have conclusively demonstrated that in youth the healthy appendix is an organ of secretion and as a consequence obstruction leads to rupture, with the appendix capable of producing a considerable amount of fluid. They also pointed out that as atrophy took place in the older patients, secretion decreased and could disappear. It is possible that in the persons included in this series, obstruction from whatsoever cause might have produced a slow rate of distention and mild inflammatory changes. This would have allowed time for adhesions to wall off the site of inflammation, and the subsequent perforation could have completed the process of atrophy so that the organ ceased to pour out sufficient fluid to spread the infection beyond the encircling adhesions. This line of reasoning was corroborated by the frequency of occurrence of flattening and fibrous replacement of the mucosa seen in the specimens (fig. 2*b*). The diseased organ, however, would have remained behind and would have been subject to recurrent mild exacerbations of inflammation leading to still further additions to the ensheathing granulomatous tissue. This possibility was supported by the frequency of occurrence of a history of intermittent attacks of pain over long periods.

**Foreign Bodies:** Intraluminal foreign bodies did not appear to be important causes of the lesions. In 1 case a nonmetallic foreign body had caused much erosion and inflammation of the wall and may well have initiated continued low grade inflammation without perforation. In another case fecaliths had been present when the appendix was previously removed.

**Atrophy and Fibrosis:** Most of the appendixes showed old chronic fibrous replacement, but it was difficult to say whether this type of process had been responsible for the initial obstructing lesions which had led to perforation and inflammation.

**Residual Stumps:** In 2 cases the appendix had been partly removed elsewhere and the granuloma had formed about the short remaining segment. In 1 the stump was filled with pus and the walls were fibrotic, thus transforming the stump into a chronic abscess. In the other the wall was not severely damaged but there was decided inflammation around the distal end as though at some time inflammatory products had leaked out at this point.

**Suture Material:** In 1 case the lesion may have resulted from the use of an excessive amount of heavy linen ligature and silk purse-string suture in removal of a gangrenous appendix. These foreign bodies

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25. Dennis, C.; Buirge, R. E.; Varco, R. L., and Wangenstein, O. H.: Studies in the Etiology of Acute Appendicitis: An Inquiry into the Factors Involved in the Development of Acute Appendicitis Following Experimental Obstruction of the Appendical Lumen of the Rabbit, *Arch. Surg.* **40**:929-948 (May) 1940.

were the focal point for the inflammation and may have formed an intramural abscess between them, as postulated by Nemilov.

**Vascular Factors:** An unusual degree of thickening of the media of the arterioles was present in 14 cases. This varied from moderate stenosis of the lumen to complete obliteration (fig. 3*b*). The exact significance of this finding could not be determined, but it was probably the result of inflammation and possibly the result of extrinsic pressure of the fibrous tissue. This process may set up a vicious cycle of necrosis and further spread of infection, as postulated by Mock.

The avascular nature of the lesions may explain the lack of systemic infection shown by the patients as a result of the absence of absorption from the inflamed tissues.

No evidence was found to support the theories of retrograde arterial thrombosis or of venous thrombosis.<sup>26</sup> The patient in case 11 did give a history of transient jaundice with his attacks, which might have been the result of low grade pylephlebitis, but this could not be proved.

**Lymphatic Vessels:** Moderate edema was found especially in the submucosa in many of the cases, but true lymphedema was not seen. Where inflammation was reasonably active, the ileocecal nodes were enlarged and were the sites of chronic inflammatory changes and fibrosis.

**Fibroplastic Diathesis:** None of the patients showed a tendency toward any other type of fibroplastic process.

**Pathologic Findings.**—The tumors exhibited varying degrees of acute, subacute and chronic inflammation. There frequently were microscopic abscesses filled with polymorphonuclear leukocytes, and at times these abscesses coalesced to form small, grossly evident abscesses. In other parts of the lesion there were foci of lymphocytes which were sometimes forming germinal follicles. In all specimens there were regions characterized by scattered infiltration with lymphocytes and monocytes and sometimes plasma cells and eosinophils. Often these cells were perivascular in distribution.

The large bulk of the mass was made up of dense fibrous connective tissue of all degrees of maturity from that of loose fibroblastic proliferation with numerous capillary buds to old, dense, avascular scar tissue. The proportion of inflammatory exudate and fibrous tissue varied greatly in different tumors. Many of the lesions evidenced thickening of the media of the arterioles, at times leading to obliteration (fig. 3*b*). The lymph nodes were the sites of only chronic inflammatory changes. The mucosa of the ileum and colon, at most, was the site of mild chronic inflammation at the points of adherence to

26. Bernard and Milone.<sup>2a</sup> Fiolle, Luccioni and Lluccia.<sup>2e</sup>

the granuloma. The granulomatous tissue sometimes extended into the muscularis and submucosa. Occasionally the ileal muscularis was hypertrophied in cases in which there was associated ileocecal obstruction.

Foreign body giant cells were rarely seen and then usually around necrotic debris which contained fragments of foreign material; this material was possibly contents of bowel which previously had been extruded. In 2 cases there were foci of fat necrosis in the involved mesentery.

Contiguity would seem to have explained the spread of infection in most cases, though the lymphatic route<sup>27</sup> was probably an accessory factor.

*Symptomatology.*—The symptoms were so varied in degree (table 3) and character that it was difficult to ascribe any set pattern to this disease process. Pain was present in all cases at one time or another. It commonly was intermittent, generalized and crampy at first, with localization in the right lower quadrant as either crampy pain or dull residual soreness lasting a few days after attacks. It had persisted for periods ranging from ten days to three years, but when present for long periods it had been so mild that medical advice had not been sought. Often there was a history of a more serious attack in the few days or few weeks preceding admission to the hospital, and when this episode had been severe an acute reactivation in the center of the mass was usually found. Crampy pains often indicated stenosis of the ileocecal valve. Two patients had pain suggestive of biliary disease, and in 2 others the pain extended to the right hip. One man denied having any pain; he had some vague discomfort in the lower abdominal region.

Nausea and vomiting were infrequent and mild, usually accompanying exacerbations of pain and subsiding in a few days.

In only 2 patients did there develop severe obstruction necessitating ileocolostomy. Nine patients had mild complaints of constipation, fulness and borborygmi, relieved by enemas or passage of flatus. One patient had slight, transient diarrhea, and 1 noted bright blood in the stool, probably due to concomitant hemorrhoids.

Seven patients had low grade fever during exacerbations,<sup>2b</sup> which subsided in a short time. Four complained of mild anorexia. Six showed a little loss of weight, while 1 man slowly lost 30 pounds (13.6 Kg.) in three years.

*Physical Findings.*—The patients were not severely ill except when recent surgical procedures had been done. The only common finding was a tender mass in the abdomen. A mass was found in 15 cases,

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27. Jamieson, J. K., and Dobson, J. F.: The Lymphatic System of the Caecum and Appendix, *Lancet* 1:1137-1143 (April 27) 1907.

a questionable mass was noted in 3 cases and no mass could be felt in 2. When present, the lump varied from the size of an egg to that of a grapefruit and was in the right middle or lower quadrant (table 3). Four patients first detected the tumor themselves, and the home physician found it in 6 others; twice the tumor was found at laparotomy. It was slightly to moderately tender in 12 patients and nontender in 4 of the 16 patients who had a mass. In addition, 1 patient had epigastric tenderness, while another had tenderness only in the epigastrium and not over the tumor. Rigidity was found once.

*Laboratory Findings.*—Hemoglobin Content and Erythrocyte Count: The degree of anemia was moderate, with an average erythrocyte count of 4,204,000. The lowest reading was 3,310,000 and the highest 4,780,000. The hemoglobin was in an equivalent range, though one reading was abnormally high at 17.9 Gm. per hundred cubic centimeters of blood (table 3).

Leukocyte Count: The leukocyte counts were suprisingly low, considering the degree of inflammation present in many cases. The average count was 10,025, and the range was from 4,600 to 17,000. In only 9 cases was the count over 10,000. In case 17, in which there was a fair-sized abscess cavity, the leukocyte count was 9,200.

Sedimentation Rate: In the 2 cases in which this test was done the results were respectively 76 and 35 mm. in one hour by the Westergren method.

Occult Blood: Tests for occult blood were made in only 4 cases. The only positive reaction was in case 6, in which the bleeding was probably due to hemorrhoids.

Urinalysis: There were no significant urinary symptoms in spite of the fact that the right ureter was close to the site of the inflammatory process in most cases; the ureter was involved in 1 case.

*Roentgenologic Diagnosis.*—Satisfactory studies of the colon were made in 15 cases. One of these studies was reported as giving negative results. In 4 cases a diagnosis of carcinoma was made (table 1).

Roentgenologic examination usually reveals evidence of an extra-cecal and extraileal mass which separates the terminal part of the ileum from the head of the cecum and displaces the latter structure to the right (fig. 4). There is frequently a smooth, convex indentation on the medial side of the cecum. The mass is palpable outside the lumens of the terminal part of the ileum and the cecum. There is usually a significant absence of the typical neoplastic changes on the mucous membrane surface of the bowel. Neoplasm will always manifest itself primarily on this surface. In order to determine these features the roentgenologist must be sure to identify the anatomic structures of the ileocecal coil. To do this he must visualize the appendix or the terminal part of the ileum, or he must be able to see the ileocecal

TABLE 3.—Summary of Clinical Findings

Onset	Severity, Grade*	Pain		Duration	Nausea*	Vomit- ing*	Obstruction *	Tem- pera- ture, F.	Tenderness, Severity, and Site	Mass, Site	Erythrocytes	Hemo- globin	Leuko- cytes
		Type	Site in Abdomen										
1	2	Intermittent sharp; stinging soreness with straining	Periumbilical shifting to right lower quadrant	8 days	0	0	Constipation, 1	0	2. Right side	Cecal region	3,960,000	....	9,200
2	1 to 2	Intermittent dull; sharp with last attack	Left upper quadrant, shifting to umbilical area and right lower quadrant	21 mo.	1	0	0	0	3. Over mass	Midabdominal region, right lower quadrant	4,290,000	78%	12,400
3	3	Intermittent crampy	Generalized	3 wk.	0	0	Borborygmi, relief with enemas	0	2. Over mass	Right lower quadrant	4,290,000	....	4,600
4	1	Intermittent mild twinges	Right lower quadrant	24 mo.	1	0	Constipation, 1; borborygmi, 1	0	2. Over mass	Right lower quadrant	4,080,000	....	17,000
5	1 to 3	Intermittent sharp; steady soreness	Generalized, right lower quadrant	36 mo.	1	1	Periodic constipation, 1	0	0. Over mass	Right lower quadrant (doubtful)	4,200,000	....	7,300
6	2 to 4	Intermittent colicky; steady soreness	Right lower quadrant and left upper quadrant	3½ mo.	0	0	Bloating and borborygmi, 1; complete obstruction	101 to 102, 1 attack	2. Pelvis	Right lower quadrant	3,310,000	....	9,800
7	1	Intermittent	Right lower quadrant	7 mo.	0	0	0	0	1. Over mass	Right lower quadrant	3,700,000	12.7 Gm.	7,400
8	1 to 2	Intermittent sharp; dull constant	Right lower quadrant	12 mo.	0	0	Bloating, 10 days	100.3, 10 days	2. Right side	Right lower quadrant	.....	....	15,900
9	1 to 3	Abdominal discomfort in lower region; severe cramps	Right lower quadrant	3 mo.	0	2; 1 wk.	0	92, 3 wk.	1. Over mass	Right lower quadrant	3,980,000	12.1 Gm.	6,900
10	1 to 2	Intermittent crampy	Midabdominal to back and scapula on right	18 mo.	0	0	Bloating, relief when flatulency passed	0	0. ....	Not present	.....	17.9 Gm.	10,900
11	2	Intermittent colicky to steady soreness	Epigastrium; right lower quadrant	12 mo.	2	2	0	Chills, fever	2. Epigastrium	Not present	.....	14.6 Gm.	10,300
12	1 to 3	Intermittent soreness	Right upper quadrant; back on right	6 mo.	0	2	Constipation, 1	0	2. Epigastrium, over mass	Right lower quadrant	3,890,000	....	6,700
13	1	Intermittent soreness	Right lower quadrant; right hip	36 mo.	0	0	0	99.3	1. Over mass	Right lower quadrant	4,240,000	68%	6,700
14	3	Intermittent sharp	Right lower quadrant	48 hr.	0	0	0	?	0. ....	Right lower quadrant	4,400,000	....	7,900
15	1	Intermittent soreness	Right lower quadrant	36 mo.	0	0	0	0	1. Over mass	Right lower quadrant	4,160,000	14.8 Gm.	11,400
16	2	Intermittent crampy to steady soreness	Generalized and in right lower quadrant	2 wk.	0	0	Distended, 3 days	0	0. ....	Right lower quadrant	4,780,000	....	9,200
17	1	Slight discomfort	Lower part of abdomen	?	0	0	0	0	0. ....	Right lower quadrant	4,290,000	76%	9,200
18	2	Intermittent grabbing and soreness	Epigastrium; right lower quadrant	8 mo.	0	0	0	0	0 to 1. Cecal region	Cecal region (doubtful)	4,560,000	....	13,700
19	3	Intermittent colicky	Lower part of abdomen	13 mo.	0	1	0	100 to 101.2, 2 wk.	0. ....	Right lower quadrant	4,560,000	75%	11,000
20	3	Intermittent cramps	Generalized, right lower quadrant	13 mo.	1	1	Complete obstruction; constipation, 2	100 to 101, 2 wk.	1. ....	Right lower quadrant (doubtful)	4,710,000	63%	13,000

\* Symptoms graded 1 to 4, with 1 representing the least and 4 the greatest severity.

valve, with filling of both the terminal part of the ileum and the cecum. A motor test meal may be necessary in addition to the barium enema but it must be remembered that the obstructive symptoms may contraindicate use of it. In none of these cases was the appendix visualized.

*Clinical Diagnosis.*—In 10 cases the primary diagnosis was carcinoma of the cecum, in 4 tumor, in 3 appendical disease, in 2 cholecystitis and in 1 an inflammatory mass, probably tuberculous (table 3). In 9 cases appendical granuloma or subacute appendicitis was seriously considered in the differential diagnosis.



Fig. 4.—Typical filling defect in the interomедial wall of the cecum, displacing the cecum laterally and the terminal part of the ileum medially. The mucosal pattern, however, is still preserved.

An accurate preoperative diagnosis is most difficult to make, and some of these tumors imitate carcinoma in almost every respect. The main diagnostic point revealed by this study was a history of intermittent attacks of moderately severe crampy pain which was often referred to as soreness in the right lower quadrant. Nausea, vomiting, fever, anorexia, loss of weight and obstruction were not common or severe. No patient complained of melena, 1 had mild diarrhea and 4 had mild constipation. A tender mass was the only physical finding. Anemia was slight, and the white blood cell count was usually slightly increased. It is possible that more frequent use of the sedimentation rate would have shown a consistent increase suggesting the inflam-



matory nature of the lesion. Also the occurrence of negative reactions to tests for occult blood in the stool would favor the diagnosis of granuloma.

*Surgical Diagnosis.*—Eleven times the surgical diagnosis was that of a malignant lesion (table 1). On five occasions the correct diagnosis was made, and in 4 cases the lesion was called "inflammatory" and was resected. Biopsy was seldom done. The reasons for not taking specimens for biopsy were the apparent conclusive gross evidence of a malignant process, the presence of partial obstruction demanding surgical intervention and the danger of soiling consequent to the taking of a sufficiently deep block of tissue to eliminate perforating carcinoma as the diagnosis.

The danger of trusting to gross appearance and superficial biopsy was illustrated in 2 cases reviewed in the course of this study. In 1 a diagnosis of encapsulated abscess of the appendix was made and ileocolostomy was done. Three months later laparotomy revealed inoperable colloid carcinoma. In the other case the appendix was removed for ligneous inflammation and three and a half years later an inoperable colloid carcinoma was found.

No evidence was found to support the contention of Bernard and Milone that in these lesions a definite line of cleavage leading to the offending appendix can be found behind the cecum.

*Course.*—It is hard to establish, from this study, what the normal course of this process is, as in all cases the process was modified by surgical interference. Certain inferences, however, can be justifiably made. There would seem to be a nice balance between continuation of the granulomatous process and resolution of the inflammatory elements, leaving a mass of dense fibrous adhesions. In all probability, case 18 illustrates a pronounced degree of spontaneous remission of a granuloma. In cases 3, 4, 6, 15 and 20 evidence of considerable involution followed ileocolostomy. In case 15 the occurrence of involution enabled the surgeon definitely to establish the appendix as the cause of the trouble at the time of the second stage, so that appendectomy alone was done. In 1 other case, the record of which was studied but was not included in the series because no tissue was available for study, a questionably malignant or inflammatory tumor, according to clinical and roentgenologic evidence, resolved so completely after ileocolostomy that the second stage was not done. Reexploration for other causes on two later occasions revealed nothing but dense fibrous adhesions.

Furthermore, in cases 12, 13, 14, 15 and 16 removal of the appendix caused clinical and, in some, roentgenologic evidence of subsidence of the tumor; this evidence in case 14 was confirmed ten years later at laparotomy.

In the absence of surgical intervention the normal course would seem to be repeated exacerbations with increase in size until obstruction takes place at the ileocecal valve or elsewhere from kinking of adherent loops of bowel.

*Treatment.*—The results of surgical intervention in these persons were gratifying. They were followed for periods ranging up to nineteen years without evidence of recurrence of trouble with the exception of the patient in case 11, who was never completely cured from the beginning (table 1).

One patient not included in this series did well after simple coring out of the appendical mucosa. Four patients were cured by means of appendectomy. One of these had intestinal obstruction from an adhesive band ten years later but remained well after that. One patient remained well after ileocolostomy and appendectomy. Six patients who underwent exteriorization procedures or two stage resections recovered and retained good health.

Two of 9 patients subjected to a one stage resection died of peritonitis, a fact which suggests that this radical procedure is dangerous in the treatment of these infectious lesions. In addition, in 1 patient there developed a pelvic abscess and fistula into the terminal part of the ileum, which continued to drain and to form abscesses for seven years, though his general health was fairly good for the first six years.

From the foregoing statements, it would seem that if the appendix can be established as the cause of the lesion, appendectomy will be curative. If the tumor can be reasonably established as inflammatory, the safest procedure is ileocolostomy or exteriorization. Shunting the fecal stream usually causes a resolution in the size of the tumor in a relatively short time. This may be sufficiently dramatic to exclude malignancy from diagnostic consideration, but careful and frequent clinical and roentgenologic rechecks are indicated to avoid missing an underlying carcinoma. Even if ileocolostomy does not resolve the question of malignancy, it almost invariably brings about sufficient reduction in the inflammatory reaction to allow for a relatively easy resection at the time of the second stage, and, as in case 15, it may make the diagnosis of appendicitis possible.

Ileocolostomy alone is not always capable of causing complete resolution, as was evidenced in case 20. Trouble repeatedly recurred because of only an infected stump of the appendix in spite of the fact that there was a properly functioning ileocolic stoma.

#### SUMMARY AND CONCLUSIONS

In a series of 20 cases of "ligneous cecitis" or "nonspecific appendical granuloma" most of the lesions were caused by perforative

inflammatory disease of the appendix. Incomplete removal of the appendix was responsible for the lesion in 2 of the cases, and an excessive amount of nonabsorbable suture was likely responsible in another.

The average age of the patients was 52.1 years. Their advanced ages probably account for the fact that their perforations were less acute than those usually seen.

The appendixes were usually located in the ileocecal angle or in the retrocecal or retroileal regions, permitting the rapid sealing off of the appendical inflammation. The tumor resulted from an extensive overgrowth of relatively avascular, inflammatory, fibrous tissue about the appendix after repeated attacks or low grade inflammation.

The combination of the three factors of age, location of appendix and the overgrowth of fibrous tissue accounted for the relatively mild local and systemic symptoms evidenced by the patients. The chief symptoms were recurrent attacks of midabdominal pain, with localization in the right lower quadrant. Anorexia, fever, loss of weight and melena were uncommon and were minimal when present.

The only consistent physical finding was a mass in the right lower quadrant of the abdomen. This was moderately tender in about half the cases. Anemia was not marked, and the leukocyte count was increased in half the cases. Sedimentation rates and tests for occult blood should help in evaluating the problem in these cases. The lesions have a characteristic roentgenologic appearance.

The diagnosis of these tumors is difficult. Carcinoma of the cecum is more common, and the possibility that the lesion is malignant should be excluded by all available methods before it is considered inflammatory. On the other hand, the lesions should be considered in the differential diagnosis of ileocecal masses, and no patient should be refused exploration on the basis of apparent local inoperability.

Surgical treatment resulted in cure of all but 1 of the patients who survived operation. Appendectomy will bring about cure if the appendix can be identified as the source of the trouble; otherwise, two stage resection would appear to be the safest treatment if the diagnosis is doubtful.

## PROGRESS IN ORTHOPEDIC SURGERY FOR 1946

A Review Prepared by an Editorial Board of the American Academy  
of Orthopaedic Surgeons

### XVII. INFANTILE PARALYSIS: RESEARCH

Prepared by  
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CLEVELAND

#### VIRUS STUDIES

SCHLESINGER and others<sup>738</sup> report that three strains of poliomyelitis virus were isolated in cases in the British Army in the Middle East. Two strains may have been related to the Lansing type, one being easily transmitted to rodents and the other being serologically of the Lansing type but not transferable; the remaining strain was not related at all and not transferable.

Olitsky and Findlay<sup>739</sup> make a similar report of a strain isolated in the case of a soldier with poliomyelitis in the Middle East. It was demonstrated that the strain could be substituted for the Lansing strain in neutralization tests in mice for epidemiologic purposes.

Kabat and others<sup>740</sup> state that the lactic acid content of the brain is significantly decreased in mice infected with the virus of poliomyelitis. This factor appears to be additional evidence for the theory that the virus may interfere in a specific manner with cell metabolism.

In his article, "Certain Properties of Theiler's Virus, Especially in Relation to Its Use as a Model for Poliomyelitis," Olitsky<sup>741</sup> concludes that differences in the original virus are such as to make it unusable as a model for the study of human poliomyelitis.

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738. Schlesinger, W.; Morgan, I. M., and Olitsky, P. K.: Transmission to Rodents of Lansing Type Poliomyelitis Virus Originating in the Middle East, *Science* **98**:452-454 (Nov. 31) 1943.

739. Olitsky, P. K., and Findlay, G. M.: The Use of the Rodent-Adapted MEF1 Strain of Human Poliomyelitis in Neutralization Tests with Serum of Apparently Normal African Natives, *J. Bact.* **52**:255-256 (Aug.) 1946.

740. Kabat, H.; Erickson, D.; Eklund, C., and Nickle, M.: Decrease in Lactic Acid Content of the Brain in Poliomyelitis, *Science* **98**:589-591 (Dec. 31) 1943.

741. Olitsky, P. K.: Certain Properties of Theiler's Virus Especially in Relation to Its Use as Model for Poliomyelitis, *Proc. Soc. Exper. Biol. & Med.* **58**:77-81 (Jan.) 1945.

Herbert S. Loring and C. E. Schwerdt<sup>742</sup> describe the method of purification of the Lansing strain of virus, and the same authors, with L. Marton,<sup>743</sup> describe the electron microscopy of the strain.

The conclusion of "Inactivation of Poliomyelitis Virus in Relation to Gastric and Intestinal Digestion," by Harold K. Faber and Luther Dong,<sup>744</sup> contains the meat of the article. The authors state that poliomyelitis virus is rapidly inactivated at the  $p_H$  levels prevailing in the stomach when only gastric juice is present and at the height of digestion of carbohydrates and of mixed meals containing meat. Pepsin contributes slightly to inactivation. The  $p_H$  levels necessary for inactivation are present in the stomach but a short part of the time, and since gastric contents are evacuated before this time unaffected virus reaches the duodenum; from then on the  $p_H$  is too high to inactivate the virus and trypsin has no effect. The authors state the belief that virus is absorbed from the intestine in this way and concentrated in the intestine, and that there is no evidence in favor of, or against, the gastrointestinal tract being the primary portal of entry. They merely have evidence that low  $p_H$  and other factors may destroy a strain of mouse-adapted virus in the stomach.

Loring<sup>745</sup> makes a correction about shapes of particles and concludes that the virus of human poliomyelitis, as cultivated in mice and cotton rats, consist of spherical particles about 25 millimicrons in diameter.

Lawson and Melnick<sup>746</sup> conclude that milk exerts a protective action against the destruction by heat of rodent-adapted virus and the virus of spontaneous poliomyelitis in mice when infected tissue from the central nervous system is heated in that medium. Suspension in milk enables these strains to withstand about 5 to 10 more centigrade degrees for thirty minutes than when the infected tissues are suspended in water. No such protection is noted when infectious intestinal contents from mice are used as a source of virus.

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742. Loring, H. S., and Schwerdt, C. E.: Isolation of a Macromolecular Constituent with Properties of the Lansing Strain of Poliomyelitis Virus, *Proc. Soc. Exper. Biol. & Med.* **62**:288-291 (June) 1946.

743. Loring, H. S.; Marton, L., and Schwerdt, C. E.: Electron Microscopy of Purified Lansing Virus, *Proc. Soc. Exper. Biol. & Med.* **62**:291-292 (June) 1946.

744. Faber, H. K., and Dong, L.: Inactivation of Poliomyelitis Virus in Relation to Gastric and Intestinal Digestion, *Proc. Soc. Exper. Biol. & Med.* **63**:575-578 (Dec.) 1946.

745. Loring, H. S.: Similarities in Electron Micrographs of Purified Lansing and SK Poliomyelitis Viruses, *Proc. Soc. Exper. Biol. & Med.* **64**:101-102 (Jan.) 1947.

746. Lawson, R. B., and Melnick, J. L.: Inactivation of Murine Poliomyelitis Viruses by Heat, *J. Infect. Dis.* **80**:201-208 (March-April) 1947.

The concentration of virus plays a role in its thermal lability. The more dilute the virus suspension the less heat is required to inactivate it, even when all dilutions are made in milk.

When concentrated suspensions of infected nerve tissues are heated for thirty minutes occasional traces of virus may be detected if the temperature is kept at 65 C. and 70 C., which is above the temperature commonly used in pasteurization (61.7 C.). However, the number of variables which affect this type of experiment is great; so unqualified didactic statements about the thermostability of these agents should not readily be made.

No information about human (monkey-adapted) poliomyelitis virus is furnished by these experiments.

[ED. NOTE.—It is my belief that the knowledge of the survival of poliomyelitis virus in milk and ice cream is inadequate.]

Brutsaert and others<sup>747</sup> conclude that propagation of human or simian strains of poliomyelitis virus is difficult in any kind of medium, although certain murine strains grow well in tissue culture containing embryonic mouse brain. From the authors' data they conclude that results at the time of their report do not encourage the assumption that neurotrophic poliomyelitis virus in stools or sewage may be maintained in symbiosis with free living microbial cells.

#### ETIOLOGY AND EPIDEMIOLOGY

Hardy<sup>748</sup> reviews the literature concerning the etiologic agent of poliomyelitis, the theories on the method of transmission of agent to host and the theories of pathogenesis in the body.

Melnick and others<sup>749</sup> report that dichlorodiphenyltrichloroethane (DDT) was applied in two areas in which there were epidemics of poliomyelitis, the areas being of about 4 square miles each and inhabited by some 67,000 and 27,000 people, respectively. Under the circumstances, which were not ideal, a temporary reduction of flies was achieved in both areas, but there was no effect on the poliomyelitis epidemic in either area.

[ED. NOTE.—The inconclusive results obtained in this work cannot be accepted without further studies.]

747. Brutsaert, P.; Jungeblut, C. W., and Knox, A.: Attempts to Propagate Murine Virus on Various Intestinal Bacteria and Protozoa, *Proc. Soc. Exper. Biol. & Med.* **61**:265-268 (March) 1946.

748. Hardy, R.: The Etiology of Poliomyelitis and the Transmission of Its Causative Agent, *Arch. Pediat.* **64**:294-313 (June) 1947.

749. Melnick, J. L.; Ward, R.; Lindsay, D. R., and Lyman, F. E.: Fly-Abatement Studies in Urban Poliomyelitis Epidemics During 1945, *Pub. Health Rep.* **62**:910-921 (June 20) 1947.

Dauer <sup>750</sup> reports on the high incidence of poliomyelitis in the United States in 1946, principally in the north central part of the country. There has been a decrease in the deaths in recent years, probably due to more complete reporting and the inclusion of a greater proportion of nonparalytic cases. Poliomyelitis was more prevalent than before in other parts of the Western Hemisphere in 1946. Epidemics appear to occur more frequently in tropical areas than is commonly stated. Accumulations of epidemiologic data in recent years appear to have strengthened the hypothesis that poliomyelitis is spread principally by person to person contact.

Melnick and Penner <sup>751</sup> had flies infected with murine-adapted poliomyelitis virus and with Theiler's TO strain of spontaneous encephalomyelitis of mice; the excreta were positive at least five days later. The excretion of carmine (biologic inert material) took place in controls in about the same time. Human poliomyelitis virus, as naturally present in the stools of patients with poliomyelitis, was fed to blow flies (*Phormia regina*); after the feeding virus was found in the flies for two weeks and in their excreta for three weeks.

Wenner and Paul <sup>752</sup> describe a fatal case of poliomyelitis which developed in a 26 year old worker in a hospital in New Haven, Conn. He had been scratched, and eight days later symptoms began to develop. It is possible that he contracted the disease naturally, but laboratory infection was a probability. The authors isolated the virus, but they point out that the portal of entry was not determined, inasmuch as the patient acquired the disease at about the time when natural infection would be suspected. Entry may have been by way of the skin, as the man had been handling infected specimens; the incubation period was rather short for the latter type of entry.

Gebhardt and McKay <sup>753</sup> conclude that data on multiple cases of poliomyelitis in families show that the condition developed at the same time in different children in the majority of families, and that in these multiple cases the children had probably obtained the virus at the same time and from the same source, suggesting means other than contact as the mode of spread. Fresh unwashed or unpeeled fruits or vegetables had been eaten in 206 of a series of 206 cases of poliomyelitis surveyed. Direct contact was traced in only 13.6 per cent

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750. Dauer, C. C.: Incidence of Poliomyelitis in 1946, *Pub. Health Rep.* **62**:901-909 (June 20) 1947.

751. Melnick, J. L., and Penner, L. R.: Experimental Infection of Flies with Human Poliomyelitis Virus, *Proc. Soc. Exper. Biol. & Med.* **65**:342-346 (June) 1947.

752. Wenner, H. A., and Paul, J. R.: Fatal Infections with Poliomyelitis Virus in a Laboratory Technician: Isolation of Virus from Lymph Nodes, *Am. J. M. Sc.* **213**:9-18 (Jan.) 1947.

753. Gebhardt, L. P., and McKay, W. M.: Transmission of Epidemic Poliomyelitis, *J. Pediat.* **28**:1-13 (Jan.) 1946.

of 241 cases surveyed. No evidence was found that water supplies, milk supplies or swimming pools were means by which the disease was disseminated. Bites of insects, such as flies and mosquitoes, suggest a possible means of the spread of virus. The closing of schools during the epidemic failed to reduce the incidence of the disease among the school age group.

Goldstein and others<sup>754</sup> state that data in the epidemic reported by them support the theory that food, possibly milk contaminated by flies, was involved. However possible, the theory is not proved.

Weaver<sup>755</sup> is unable to show any evidence that diets deficient in vitamin A affect the susceptibility or resistance of cotton rats to poliomyelitis when the disease is introduced in the usual ways (intracerebrally or by instillation, ingestion or contact). Cotton rats with deficient diets were more susceptible to the introduction of poliomyelitis by the intratonsillar route, by intracolonic and intranasal instillation and by subcutaneous and intracardiac injection.

Gear and others<sup>756</sup> were able to isolate poliomyelitis virus from the first outflow of sewage in the settlement tanks at Johannesburg, South Africa, although a second sample from the final effluent, after sand filtration, was negative.

Bigelow<sup>757</sup> presents the hypothesis that poliomyelitis is not a disease entity but a complication of influenza. The article is an interesting one because early influenza does look like poliomyelitis, but no student of poliomyelitis imagines that the two are the same disease.

"Epidemiological and Experimental Observations of Poliomyelitis in New York City," by Jungeblut and Dalldorf,<sup>758</sup> contains a small error, which is corrected in a subsequent article.

Kessel and others<sup>759</sup> demonstrate that strains of poliomyelitis differ in virulence when the *Macaca mulatta* is used and the inoculation made intracerebrally. Antigenic differences occur, but these may be relative in character.

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754. Goldstein, D. M.; Hammon, W. M., and Viets, H. R.: Outbreak of Polioencephalitis (with Poliomyelitis) Among Navy Cadets, Possibly Food Borne, *J. A. M. A.* **131**:569-573 (June 15) 1946.

755. Weaver, H. M.: Resistance of Cotton Rats to Virus as Affected by Intake of Vitamin A, Partial Inanition and Sex, *J. Pediat.* **28**:14-23 (Jan.) 1946.

756. Gear, J.; Mundel, B., and Wilson, D.: Isolation from Sewage in Johannesburg, South African M. J. **20**:139-140 (March 23) 1946.

757. Bigelow, O. P.: Anterior Poliomyelitis a Complication of Influenza, *J. Indiana M. A.* **39**:72 (Feb.) 1946; Infantile Paralysis a Complication of Influenza, *Ohio State M. J.* **42**:499 (May) 1946.

758. Jungeblut, C. W., and Dalldorf, G.: Epidemiological and Experimental Observations of Poliomyelitis in New York City, *Am. J. Hyg.* **43**:49-64 (Jan.); erratum, **43**:194-209 (March) 1946.

759. Kessel, J. F.; Moore, F. J., and Pait, C. F.: Differences Among Strains in *Macaca Mulatta*, *Am. J. Hyg.* **43**:82-89 (Jan.) 1946.



Melnick and Ward<sup>760</sup> tested flies trapped in four epidemic areas for poliomyelitis virus and demonstrated its presence in vervet monkeys in urban Chicago and in North Carolina.

Hovanic<sup>761</sup> reviews the question of the portal of entry in poliomyelitis.

Stokes<sup>762</sup> reports a case in a mother delivered of a live normal baby by cesarean section three minutes after her death.

Toomey and others<sup>763</sup> describe a strain of virus isolated from creek water by direct transmission to the cotton rat.

Muller<sup>764</sup> states that according to Petersen, the accumulation of cases of poliomyelitis after the autumnal equinox is the result of decreased resistibility; the exact cause is believed to be the great reduction in radiation during September and October, accompanied with a decrease in the length of the days. According to this hypothesis, the resistibility is a photoperiodic reaction in analogy with various remarkable reactions known in plants and animals.

Wenner,<sup>765</sup> in an epidemiologic study of poliomyelitis in Alabama, noted that rates of incidence were highest in epidemic years in northern rural counties consisting of villages and incorporated towns.

McFarlan,<sup>766</sup> in a short note on the epidemic in the island of Mauritius, mentions that there was a great prevalence of intestinal disease preceding the epidemic and that the epidemic itself occurred shortly after a cyclone, which created terrible sanitary conditions.

Gear and Mundel,<sup>767</sup> who studied an epidemic occurring in Johannesburg, South Africa, conclude that direct personal contact during the incubation period in 1 patient caused the spread. The statement is made that the original patient was excreting virus in the feces twelve days before symptoms appeared. Many exposed persons excreted virus, though they were otherwise unaffected.

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760. Melnick, J. L., and Ward, R.: Poliomyelitis: Susceptibility of Vervet Monkeys to Virus in Flies Collected at Epidemics, *J. Infect. Dis.* **77**:249-252 (Nov.-Dec.) 1945.

761. Hovanic, K. J.: Portal of Entry of Poliomyelitis, *Arch. Pediat.* **62**: 563-581 (Dec.) 1945.

762. Stokes, E. M.: Poliomyelitis: Failure of Intrauterine Fetal Transmission, *J. Oklahoma M. A.* **39**:153-154 (April) 1946.

763. Toomey, J. A.; Takacs, W. S., and Weaver, H. M.: Isolation of Poliomyelitis Virus from Creek Water by Direct Transmission to Cotton Rat, *Am. J. Dis. Child.* **70**:293-297 (Nov.-Dec.) 1945.

764. Muller, D.: Reason for Outbreak of Poliomyelitis During Autumn Equinox, *Acta med. Scandinav.* **122**:170-174, 1945.

765. Wenner, H. A.: Poliomyelitis in Alabama: Epidemiologic Considerations, *Yale J. Biol. & Med.* **18**:281-306 (March) 1946.

766. McFarlan, A. M.: Epidemiology of 1945 Outbreak in Mauritius, *Proc. Roy. Soc. Med.* **39**:323-324 (April) 1946.

767. Gear, J., and Mundel, B.: Poliomyelitis: Outbreak Occurring in Suburb of Johannesburg, *South African M. J.* **20**:106-110 (March 9) 1946.

Findlay and others<sup>768</sup> conclude that poliomyelitis is endemic in West Africa but rare in West African soldiers; the incidence among Europeans is greater than among Africans, and greater in officers than in the ranks. The authors describe a fatal case in which virus was recovered; several strains of monkeys were responsive. It is stated that the serums of West Africans contain immune bodies to the Lansing strain.

Conway and Bigwood<sup>769</sup> give a striking report of an epidemic in which the rate of incidence was calculated to be 288.6 cases per 100,000 persons, in striking contrast to the previous average rate of 7.5 per 100,000. Contact between patients was traced in only 28 per cent of cases. The authors have written an exhaustive article, in which it is stressed that the theory of person to person spread must be considered in the nature of a diagnosis by exclusion and that firm establishment of a diagnosis depends on a more thorough elimination of other possible explanations of the epidemiology of poliomyelitis.

Collins<sup>770</sup> concludes:

Poliomyelitis as reported to health departments in the past 15 years shows an epidemic situation in some region of the United States during nearly every year. The periods of exceptionally high incidence usually extended over 2 years in which the western part of the country tends to have high rates in one year and the eastern part in the other. There is great variation in the heights of the peaks in the several geographic sections in terms of cases per 100,000 population. The peak rates tend to occur somewhat earlier in the South than in the North and West. The years 1943 and 1944 both had high rates and in 1945 rather large numbers of cases were reported in most of the geographic sections.

In house-to-house canvasses made a few years ago, family informants (usually mothers) reported that 5.7 per 1,000 living children 15-19 years of age had a history of poliomyelitis at some time since birth. Not all of the reported histories were paralytic; at 15-19 years of age 4.5 per 1,000 living children gave a history of a paralytic attack, and 3.0 per 1,000 had residual paralysis or muscle weakness.

History rates of poliomyelitis were reported as rather consistently higher in Northeast and North Central cities than in the South. Histories of poliomyelitis were exceptionally high in the West but when paralytic cases with residual effects are considered, the West shows lower history rates than the North Central section. . . .

Data from a family survey on the character of the crippling effects of poliomyelitis indicate that the legs are most frequently affected. Crippling involved

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768. Findlay, G. M.; Anderson, J. R., and Haggie, M. H. K.: Poliomyelitis in West Africa, *J. Roy Army M. Corps* **86**:20-25 (Jan.) 1946.

769. Conway, J. A., and Bigwood, D. E., Jr.: Observations Made During Epidemic in 1944 in Hornell State Health District, New York, *New York State J. Med.* **46**:275-289 (Feb. 1) 1946.

770. Collins, S. D.: The Incidence of Poliomyelitis and Its Crippling Effects, as Recorded in Family Surveys, *Pub. Health Rep.* **61**:327-355 (March 8) 1946.

the feet or legs in 85 percent of the children under 15 years of age with residuals of poliomyelitis, as compared with 25 percent which involved the hands or arms; in a considerable proportion of the cases both the legs and arms were involved. Involvement of only the fingers or toes was negligible.

The age incidence of poliomyelitis is more similar to that of diphtheria than of scarlet fever or whooping cough. The peak rate in the survey data occurred at 3 years of age, with a fairly regular decline in incidence as age increased. Unlike most diseases, relative variation with age was greater in poliomyelitis case rates than in death rates.

Both incidence and mortality indicate somewhat lower poliomyelitis rates among girls than boys. Measures of the severity of the disease, such as the proportion of cases that were paralytic, indicate that the disease is slightly less severe in girls than boys. This is the opposite of the showing for diphtheria and is quite different from scarlet fever in which the incidence was practically identical for girls and boys.

Poliomyelitis case and death rates were lower for colored than for white persons living in the same geographic section.

Poliomyelitis death rates in the United States among residents of cities of various sizes indicate that the rate increases as size of city decreases, but rural areas and villages under 2,500 have lower rates than small cities and higher rates than cities of 100,000 and over. This general pattern holds true in the several geographic regions.

Cases recorded in the family survey were checked by name against health department files of reported cases in each of the 28 cities included. Also total cases for whole populations of the surveyed cities were estimated from the canvassed samples and compared with cases reported to the health departments. These two methods indicate that from 74 to 86 percent of poliomyelitis cases were reported to the health departments. . . . In the Northeast where the disease was definitely epidemic during the study year, a higher proportion of the cases was reported than in areas remote from the center of the outbreak.

Horstmann and others<sup>771</sup> studied 20 patients in an epidemic. Virus was isolated from 1 of 19 pharyngeal smears, 1 of 15 oropharyngeal washings and 7 of 10 stools during the first week. During the second week none of 6 pharyngeal smears, none of 7 oropharyngeal washings and 4 of 7 stools yielded virus.

Melnick, Horstmann and Ward<sup>772</sup> studied the blood, oropharyngeal washings and stools of 75 patients in contact with persons with poliomyelitis, in a search for possible virus. The specimens were divided into thirteen pools of each type of specimen. No virus was detected in the blood pools; one pool of oropharyngeal washings and three of stools were positive.

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771. Horstmann, D. M.; Melnick, J. L., and Wenner, H. A. Isolation of Poliomyelitis Virus from Human Extra-Neural Sources: Comparison of Virus Content of Pharyngeal Swabs, Oropharyngeal Washings and Stools of Patients, *J. Clin. Investigation* **25**:270-274 (March) 1946.

772. Melnick, J. L.; Horstmann, D. M., and Ward, R.: Isolation of Poliomyelitis Virus from Human Extra-Neural Sources: Comparison of Content of Blood, Oropharyngeal Washings and Stools of Contact, *J. Clin. Investigation* **25**: 275-277. (March) 1946.

In another study the same authors<sup>773</sup> demonstrated virus in stools in 70 per cent of 61 cases in the first two weeks after onset, in 50 per cent in the third and fourth weeks, in 27 per cent in the fifth and sixth weeks and in 13 per cent in the seventh and eighth week; in 1 instance, virus was present during the twelfth week after onset. No virus was obtained in 23 specimens collected from the thirteenth to the twenty-fourth week. Whether the patients were paralytic or not made no difference in the presence of virus.

In a third article, Ward, Horstmann and Melnick<sup>774</sup> report the results of blood tests on 111 patients with poliomyelitis, made in the light of more recent methods of purification; only 1 test gave positive results.

#### PATHOLOGY AND PHYSIOLOGY

Fischer,<sup>775</sup> in a study of the function of the spinal cord and poliomyelitis, states that lesions appear everywhere in the central nervous system, though usually in the motor systems; lesions of the cord are commonest in the internuncial areas. A lack of correlation between symptoms and actual damage is pointed out. Only two groups reported results of research on early changes in muscles. Fischer states the opinion that of all the concepts of Sister Kenny that of spasm seems to be the most acceptable. He concludes:

The problems of muscle function in poliomyelitis are further complicated by the fact that as a rule not all motor units of an anatomic muscle are involved in the same way and to the same extent by all the possible mechanisms outlined. Nevertheless, present knowledge of the physiology of the central nervous system and of the nature of distribution of the lesions in poliomyelitis permits one to visualize some of the probable mechanisms involved in the causation of the observed symptoms. Since the internuncial neurons, which are of such importance according to the newer physiologic concepts, are not always at the same spinal cord levels as the anterior horn cells connected with the affected muscles, it becomes understandable why often the level of damage in the spinal cord does not correspond to the level from which the motor nerves originate.

The pattern of distribution of the histologic lesions of poliomyelitis was studied by Luhan<sup>776</sup> in 13 fatal cases which were predominantly instances of the "bulbar" type of the disease. The cases occurred in

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773. Horstmann, D. M.; Ward, R., and Melnick, J. L.: Isolation of Poliomyelitis Virus from Human Extra-Neural Sources: Persistence in Stools After Acute Infection, *J. Clin. Investigation* **25**:278-283 (March) 1946.

774. Ward, R.; Horstmann, D. M., and Melnick, J. L.: Isolation of Poliomyelitis Virus from Human Extra-Neural Sources: Search for Virus in Blood of Patients, *J. Clin. Investigation* **25**:284-286 (March) 1946.

775. Fischer, E.: Modern Physiologic Concepts of Spinal Cord Function and Poliomyelitis, *Arch. Phys. Med.* **27**:333-338 (June) 1946.

776. Luhan, J. A.: Epidemic Poliomyelitis, *Arch. Path.* **42**:245-260 (Sept.) 1946.

the Chicago epidemic of 1943. Involvement of the gigantocellular layer of the motor cortex was noted in 12 of the 13 cases. This observation is in conformity with the findings in several previous investigations and is evidence of the presence of a systemic factor in poliomyelitis. The observation is also a clue to the identification of the virus, so far as identification may be ventured from the exhibition of pathologic changes in the central nervous system. The olfactory route was probably not the important channel of inoculation in these cases. The author notes that certain caprices of histologic reactions may be encountered in human poliomyelitis.

Watson and others<sup>777</sup> state that the white matter of the central nervous system of warm-blooded animals contains small amounts of coproporphyrin. Occasionally hypertension occurs in acute porphyria, which commonly affects the central nervous system. The authors studied 64 cases of poliomyelitis. They state:

A considerable excess in the excretion of coproporphyrin III has been commonly noted in a series of urine samples from cases of acute poliomyelitis. The total urinary coproporphyrin is usually in the range of 100-500  $\gamma$  per 24-hour sample, with from 50-90% of Type III isomer, as compared with 20-100  $\gamma$  and 8-35%, normally.

Carey and others<sup>778</sup> conclude:

One factor in the atrophy of disuse of muscle appeared . . . to be the substantial loss of the discharge of neurosomes into muscles as well as the quantitative decrease of the myoplasm. The giant fusiform neurosomes that appear during the early period following tenotomy disappear when the living muscle *in situ* is adequately restretched prior to excision and gold implantation.

Melnick and Horstmann<sup>779</sup> found that a specific strain of poliomyelitis virus, when administered subcutaneously or orally to chimpanzees, caused a subclinical infection of the gastrointestinal tract lasting about two weeks and that neutralizing antibodies appeared subsequently in the serum.

A second experiment showed that the immunity following the infection was sufficient to prevent the presence of the virus in feces after the subcutaneous injection of similar strains three months later.

Another experiment showed that when the animals had had one infection their subsequent immunity was such that on feeding the

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777. Watson, C. J.; Schulze, W.; Hawkinson, V., and Baker, A. B.: Coproporphyrinuria in Acute Poliomyelitis, *Proc. Soc. Exper. Biol. & Med.* **64**: 73-78 (Jan.) 1947.

778. Carey, E. J.; Haushalter, E.; Massopust, L. C.; Garofalo, F.; Lynch, J.; Tabat, D., and Socoloff, E.: Effects of Use and Disuse on Nerve Endings, Neurosomes and Fiber Types in Skeletal Muscle, *Proc. Soc. Exper. Biol. & Med.* **64**:193-200 (Feb.) 1947.

779. Melnick, J. L., and Horstmann, D. M.: Active Immunity to Poliomyelitis in Chimpanzees Following Subclinical Infection, *J. Exper. Med.* **85**:287-303 (March 1) 1947.

similar strain orally, virus was recovered from the feces for a period of only two days, whereas after the first administration the virus had been recovered over a two week period.

The authors state:

This report is concerned with the production of subclinical poliomyelitis in the chimpanzee, and immunity to such infection. Subclinical infection was produced in eight chimpanzees by the administration of virus orally or intracutaneously, and was measured by the production of a virus carrier state and the development of neutralizing antibodies. Immunity was tested by attempting to induce the carrier state again by a challenge dose of virus by the same routes.

With an homologous strain as the challenge virus, immunity as defined here was produced in each of four chimpanzees tested. Neutralizing antibodies to the homologous strain were present about 1 month following the first exposure to virus by either the oral or cutaneous route.

In another group of two chimpanzees, one developed neutralizing antibodies and immunity to heterologous strains, and one did not.

Bodian and Howe<sup>780</sup> state that no correlation could be made between lesions of the peripheral ganglions in infected and noninfected chimpanzees. In serial sections in fatal cases in human beings there were no significant lesions in stellate or celiac ganglions, but in trigeminal and spinal sensory ganglions there were both neuronal and infiltrative lesions, suggesting a spread of virus centrifugally from the central nervous system. The authors state the belief that it is doubtful that lesions in sympathetic ganglions are specifically due to poliomyelitis.

The authors conclude:

This hypothesis, which we have previously presented and discussed, is that the V, VII, and IX cranial nerves, serving the oropharynx, and the X cranial nerve supplying the lower alimentary tract are the most likely routes of passage of virus to CNS, according to the present state of our knowledge. The mucous membranes supplied by these nerves, moreover, are the only ones shown regularly to contain virus in man.

Two principal difficulties in the interpretation of histopathological findings in peripheral ganglia were revealed by this study. The first is that the specificity of lesions in sympathetic ganglia had not been established beyond doubt as being due to poliomyelitis. The second is that the presence of characteristic lesions in sensory ganglia does not, and cannot, reveal whether the virus reached the ganglia from the periphery or from the central nervous system, except in very early preparalytic stages or in exceptional cases of early arrest of virus spread and of lesion production.

Hodes<sup>781</sup> demonstrates associated peripheral nerve defects in poliomyelitis. The author states the belief that the concepts of pathology

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780. Bodian, D., and Howe, H. A.: The Significance of Lesions in Peripheral Ganglia in Chimpanzee and in Human Poliomyelitis, *J. Exper. Med.* **85**:231-242 (March 1) 1947.

781. Hodes, R.: Electromyographic Studies of Human Poliomyelitis, *Am. J. M. Sc.* **213**:509-510 (April) 1947.

must be broadened to include both peripheral and central nervous system structures, and especially structures that have anything to do with movement.

Luft and Müller<sup>782</sup> examined 66 persons, 54 of whom had acute poliomyelitis during 1944 and 1945, and 12, during the period of 1934 to 1936; endocrine disorders were observed in 20 of these patients, all of whom were women. The endocrine disorders varied to a large extent; there were menstrual disorders in 8 patients, changes of body weight in 11, disturbances of sexual and bodily development in 3 and increased thirst in 3. Decreased dextrose tolerance was demonstrated in 14 cases in which tests were performed. Hypertrichosis was present in 24 cases; it was most common in those in which there was pronounced paresis of the extremities. In several cases, the hypertrichosis was probably a manifestation of a trophic disorder following the injury of the peripheral neuron. Mental disorders were observed in 36 of the 66 patients. Those who had poliomyelitis as adults showed mental disorders of the organic neurasthenic type. In 4 of the 7 patients who had the disease during childhood, a change of personality was noticed. The frequency of mental disorders was equal in children and in adults.

Physical invalidity was of little importance in the development of mental disorders. There was no correlation between clinical signs of encephalitis during the acute stage of poliomyelitis and the appearance of endocrine or mental disorders in the after-stage. Endocrine and mental disorders appeared independently of each other. The pathologico-anatomic basis of the endocrine and mental disorders is obscure; they may be considered as manifestations of inflammatory changes in the hypothalamus.

Robinson<sup>783</sup> states the theory that pressure from edema produces spasm, pain and paralysis and that most patients with high temperature have involvement of the thermal center; general dehydration presents a logical early treatment for relief.

Holtman<sup>784</sup> states that seasonal temperature fluctuations and resulting metabolic disturbances, particularly a decrease in metabolic rate, may be considered as being more conducive to susceptibility than prolonged exposures to relatively high, yet stable, temperatures.

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782. Luft, R., and Müller, R.: Endocrine and Mental Disorders in Acute Anterior Poliomyelitis, *Acta med. Scandinav.* **127**:448-450 (May 10) 1947.

783. Robinson, T. E.: Poliomyelitis: Observations on Etiology, Pathology and Symptomatology, *Rocky Mountain M. J.* **43**:119-123 (Feb.) 1946.

784. Holtman, D. F.: Effect of Environmental Temperature on Mouse Susceptibility to Poliomyelitis Virus, *Science* **103**:137-138 (Feb. 1) 1946.

Bodian<sup>785</sup> notes that muscular rigidity, associated with hyperflexion, often precedes flaccid paralysis. [ED. NOTE.—The only fault with this statement is that the phenomenon is not a clinical fact.] The so-called muscle spasticity is a phenomenon occurring with increased stretch reflexes, but one which occurs late, or relatively so, and may not occur at all. Tremor is mentioned; it is not a common factor in clinical poliomyelitis, though fasciculation is. Material from three specimens was injected intracerebrally into experimental animals; since the animals showed spasticity in the legs without the presence of lesions in the lumbar portion of the cord, it is concluded that lesions in the brain alone can produce the spasticity of acute poliomyelitis.

Flynn<sup>786</sup> describes the clinical course of the disease and the autopsy record in the case of a man of 25 who died of poliomyelitis. Of interest is the photograph showing severe atrophy of degeneration.

#### TREATMENT

Nelson<sup>787</sup> relates all factors to be considered in evaluating effective treatment in poliomyelitis. The author notes that when cases are to be compared the points of examination in the course of illness should be the same and that when percentage of improvement is to be calculated patients must of necessity have been ill for about equal lengths of time. He also states that comparisons between two groups of patients should be made only on corresponding muscles with similar degrees of involvement. Fallacies creep in when different groups of muscles are compared. Unless such factors are taken into consideration, a treatment which has no effect on the paralysis of poliomyelitis may appear to yield remarkable results when administered to patients with mild degrees of paralysis early in the disease, whereas the application of the same treatment to the same patients later in the disease, or to patients with severe paralysis, may appear actually to do harm; in neither case would the true picture be obtained.

Buchanan and his associates<sup>788</sup> describe a simplified program that could be established in any general hospital. The paper should be consulted for details.

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785. Bodian, D.: Experimental Evidence on Cerebral Origin of Muscle Spasticity in Acute Poliomyelitis, *Proc. Soc. Exper. Biol. & Med.* **61**:170-175 (Feb.) 1946.

786. Flynn, J. E.: Sudden Death During Clinically Convalescent Stage of Anterior Poliomyelitis, *J. Iowa M. Soc.* **36**:103-105 (March) 1946.

787. Nelson, N. B.: Factors to Be Considered in Evaluating Effect of Treatment in Anterior Poliomyelitis with Special Reference to Improvement in Muscle Strength, *Arch. Phys. Med.* **28**:358-363 (June) 1947.

788. Buchanan, J. J.; Hirt, S., and Wrisley, F.: A Poliomyelitis Program in a General Hospital, *Arch. Phys. Med.* **28**:289-294 (May) 1947.



Lichstein and others<sup>789</sup> studied the influence of pyridoxine, inositol and biotin deficiencies on the effect of poliomyelitis in over 1,400 mice but could find no striking difference in susceptibility to either Lansing's strain of poliomyelitis or Theiler's strain of encephalomyelitis; neither was there any effect when the animals were fed optimal amounts of these vitamins.

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## XVIII. NEUROMUSCULAR DISORDERS EXCLUSIVE OF POLIOMYELITIS

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*Cerebral Palsy.*—The literature reviewed for the year 1946 on the subject of cerebral palsy, though revealing an increasing interest in the treatment of this condition, fails to disclose any particularly new or promising departures from the usual approaches to the problem. It is encouraging that the trend is away from the surgical forms of treatment and toward a more rational routine of muscular reeducation, augmented, when necessary, by judicious and carefully planned surgical intervention. It is important for all who deal with this condition to realize that there is no one method of treatment which can be employed to the exclusion of the others and that no single program of treatment can be employed in all cases of cerebral palsy. The interested surgeon is referred to Phelps's paper,<sup>790</sup> in which the incidence and distribution of cases as to locality and economic level are given and the underlying etiologic factors, the indications for rehabilitation and surgery and the use of drugs are discussed.

[ED. NOTE (W. M. P.).—Certain favorable impressions in regard to the value of neostigmine U. S. P. (prostigmin methylsulfate®) in the treatment of cerebral palsy, as recorded in this paper, have, unfortunately, not been substantiated by further clinical trial. Neostigmine is now employed by the reviewer only in certain cases of rigidity and true spasticity, and the results even in these carefully selected cases have, in the main, been disappointing.]

789. Lichstein, H. D., and others: Influence of Pyridoxine, Inositol and Biotin on Susceptibility of Swiss Mice, *Proc. Soc. Exper. Biol. & Med.* **60**:279-284 (Nov.) 1945.

790. Phelps, W. M.: Recent Significant Trends in Care of Cerebral Palsy, *South. M. J.* **39**:132-138 (Feb.) 1946.

Fay,<sup>791</sup> in a paper on rehabilitation of movement in patients with cerebral palsy, discusses the necessity for a complete evaluation of the condition of a child with cerebral palsy at the beginning of treatment. This procedure should include a complete neurologic, orthopedic and mental study, and should permit concentration on practically obtainable goals, with the curtailment of useless treatment. Fay briefly describes his approach to rehabilitation with physical therapy from a phylogenetic standpoint, which is in contrast to Phelps's ontogenetic approach.

[ED. NOTE.—Fay, a neurosurgeon, has developed a novel and valuable approach to the problems of cerebral palsy and the treatment of the various manifestations of this condition. It is hoped that a more detailed exposition of this approach will be made available in the literature in the near future.]

In another paper,<sup>792</sup> Fay describes the "high spinal spastic" condition in which the lesion is located at the level of the decussation of the pyramids and is usually the result of birth trauma. This condition must be differentiated from the "cerebral spastic" type and when diagnosed early may be partially or completely relieved by surgical decompression of the posterior ring of the atlas and axis. The author also discusses briefly the physical rehabilitation of the patient with cerebral palsy.

[ED. NOTE.—This paper is an excellent, though brief, discussion of a type of spastic palsy which is rarely differentiated from the true cerebral palsy.]

Denhoff,<sup>793</sup> Evans,<sup>794</sup> Collis and Buck,<sup>795</sup> Dowd,<sup>796</sup> House and Zeiter<sup>797</sup> and House and Martiny<sup>798</sup> have written papers of a general nature, which briefly discuss various phases of the problem of cerebral palsy, such as classification, diagnosis, treatment and the requirements for a training program for the patients. These papers, though excellent

791. Fay, T.: Observations on Rehabilitation of Movement in Cerebral Palsy Problems, West Virginia M. J. **42**:77-80 (April) 1946.

792. Fay, T.: Problems of Rehabilitation in Patients with Cerebral Palsy, Delaware State M. J. **18**:57-60 (March) 1946.

793. Denhoff, E.: Progress in Cerebral Palsy, Rhode Island M. J. **29**:505-509 (July) 1946.

794. Evans, E. S.: Cerebral Palsy, Proc. Roy. Soc. Med. **39**:317-320 (April) 1946.

795. Collis, E., and Buck, M. C.: Treatment of Cerebral Palsy, J. Ment. Sc. **92**:421-424 (April) 1946.

796. Dowd, H. L.: There Is Hope for Victim of Cerebral Palsy, New York Med. **2**:21-22 (April 20) 1946.

797. House, F. B., and Zeiter, W. J.: Treatment of Cerebral Palsy, Cleveland Clin. Quart. **13**:213-217 (Oct.) 1946.

798. House, F. B., and Martiny, R. J.: Occupational Therapy in Treatment of Congenital Athetosis, Cleveland Clin. Quart. **13**:218-220 (Oct.) 1946.

summaries, contribute little that is new to knowledge of the problem. Usher,<sup>799</sup> in a short paper, considers the social aspects of the problem of the child with cerebral palsy, such as his attitude toward others and toward himself, as well as the proper attitude of the parent toward the child.

[ED. NOTE.—This is an excellent, though brief, discussion of a neglected phase of the problem.]

McIntyre<sup>800</sup> reports the results of a study of 287 children with cerebral palsy, with regard to the distribution of their physical handicap in correlation with their mental capacity. He observed that the incidence of mental defectiveness among patients with right hemiplegia was approximately twice as great as that among those with left spastic hemiplegia, and that among patients with quadriplegia mental defectiveness was twice as common in those whose handicap was greater on the right side than on the left.

[ED. NOTE.—This study brings out that mental retardation amounting to borderline intelligence or to feeble-mindedness occurs more frequently when the handicap is present only on the right side or is more pronounced on that side. The evidence indirectly corroborates Phelps's finding regarding both laterality of cerebral function and the relations of handedness, speech development and localization of cerebral lesions.]

Kabat and Jones<sup>801</sup> review the literature in regard to the effects of neostigmine in the treatment of various neuromuscular disturbances, including poliomyelitis, hemiplegia and spastic cerebral palsy.

They report the results observed in 32 cases of chronic spastic paralysis and related conditions due to cerebral lesions. At the time neostigmine therapy was begun, all other types of treatment for the paralysis were discontinued. The dose of the injections varied from 1 cc. of a 1:2,000 solution of neostigmine methylsulfate U. S. P. (0.5 mg.) with  $\frac{1}{200}$  grain (0.32 mg.) of atropine sulfate U. S. P. to 3 cc. of 1:2,000 solution of neostigmine methylsulfate (1.5 mg.) with  $\frac{1}{100}$  grain (0.65 mg.) of atropine sulfate; the injections were given six times a week (once daily, excluding Sunday). In a few cases, neostigmine bromide U. S. P. was given orally to supplement the injections, in a dosage of 15 mg. three times per day (45 mg.) with  $\frac{1}{150}$  grain (0.4 mg.) of atropine sulfate at the same time. In 11 cases of hemi-

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799. Usher, E.: Integrated Approach to Cerebral Palsy, Delaware State M. J. **18**:196-199 (Sept.) 1946.

800. McIntire, J. T.: Incidence of Feeble-Mindedness in the Cerebral Palsied, Am. J. Ment. Deficiency **50**:491-494 (April) 1946.

801. Kabat, H., and Jones, C. W.: Studies on Neuromuscular Dysfunction: Neostigmine Therapy of Chronic Spastic Paralysis from Cerebral Lesions, J. Nerv. & Ment. Dis. **103**:107-129 (Feb.) 1946.

plegia of more than one year's duration, all patients showed definite improvement, the duration of the paralysis appearing not to influence the response. In these cases the improvement consisted in (1) decrease in spasticity, (2) facilitation of voluntary motion and (3) facilitation of sensory function. Kabat acknowledges that the most that can be expected from neostigmine therapy is the facilitation of formation of new pathways through the remaining undamaged portion of the central nervous system. In 8 cases of hemiplegia of less than one year's duration, the response was varied. Of those patients with the spastic type of cerebral palsy, 3 children showed significant improvement, 1 adult slight improvement and 2 adults no improvement. Three adults with the athetoid type of cerebral palsy showed significant improvement, as did 2 children with the ataxic type. Patients with miscellaneous conditions, including acoustic neuroma, anastomosis of the spinal accessory nerve, cervical disk, injury to the spinal cord and pseudotrophic muscular dystrophy, showed little or no improvement.

In a series of 25<sup>a</sup> patients with cerebral palsy, Jepson<sup>802</sup> reports encouraging results with the use of neostigmine combined with intensive reeducational physical therapy. The younger the patient at the time drug therapy was begun, the more likely was neostigmine to produce beneficial results. Jepson states that he prefers small doses, given more frequently during the day, to larger, less frequently administered doses. It is his opinion that the drug should be administered for at least six months, for if it is discontinued at the end of two or three months there is a partial recurrence of the former spastic symptoms.

Pohl<sup>803</sup> reports on a series of 10 children with cerebral palsy, some of whom had the true spastic form and some the athetoid form of the condition, to whom neostigmine was administered for a period of six months; 8 of the children had been under physical treatment for several years prior to the study. In none of the 10 children was there objective evidence of improvement which could be attributed to the drug, though 3 patients stated that they felt more relaxed during the period of medication.

[ED. NOTE.—My experience with a large number of patients with cerebral palsy has not verified the enthusiastic results of Kabat and Jones<sup>801</sup> and of Jepson.<sup>802</sup> It has been my experience that the use of neostigmine has not effectively facilitated the training-in of motor patterns over undamaged nerve pathways to any appreciable extent.

802. Jepson, P. N.: Use of Prostigmin in Management of Infantile Cerebral Paralysis, *J. Pediat.* 28:65-68 (Jan.) 1946.

803. Pohl, J. F.: Effect of Prostigmin in Cerebral Palsy, *Minnesota Med.* 29:419-422 (May) 1946.

It is essential, if the effectiveness of the drug is to be accurately determined, that a valid system of controls be instituted, including a period of muscular reeducation and training prior to administration of the drug, during which graphs of the patient's progress are maintained; it is also of importance to determine whether the progress of the patient is maintained at an accelerated rate after discontinuance of the neostigmine. Obviously, it is impossible to use separate patients as controls, since the rate of progress is different for each individual patient. I, too, have noted that some patients feel more relaxed during the period of medication, particularly in regard to the "small muscles," such as those of the hands and the tongue.]

Seidler,<sup>804</sup> in a short paper, discusses Stoeffel's selective resection of the peripheral nerve fibers to the flexor carpi radialis and the pronator teres, the intrapelvic resection of the obturator nerve for spasticity and deformity of the adductor muscles and resection of the branches of the popliteal nerve to the gastrocnemius muscle, both in conjunction with lengthening of the hamstring tendons and alone. Lengthening of the achilles tendon or fasciotomy\* of the gastrocnemius muscle should not be performed at the same time as the resection of the nerve, since lengthening of the tendon impairs the excursion of the joint and the gait in proportion to the degree of lengthening.

[ED. NOTE.—Before neurectomy or tendon lengthening is performed, it is essential that the status of the antagonists be accurately determined. For example, if there is any degree of spasticity of the dorsiflexors of the foot or ankle, popliteal neurectomy or lengthening of the achilles tendon may well result in a secondary deformity of the calcaneus.]

De Lange<sup>805</sup> discusses dystonia musculorum progressiva in a thorough fashion. This puzzling and relentlessly progressive condition is, fortunately, rather uncommon, but it is an entity which should be kept in mind so that it may be diagnosed early in the course of its development. Curman<sup>806</sup> discusses briefly the various aspects of this disease; in addition, Wilson's progressive lenticular degeneration is considered.

*Paraplegia.*—As a result of experiences in World War II, there are now appearing an increasing number of papers which deal with the various aspects of the rehabilitation of patients paralyzed as a result of injuries to the spinal cord. The methods of therapy are undergoing radical changes and include care of decubitus ulcers, and treatment of

804. Seidler, F.: Treatment of Spastic Paralysis with Special Reference to Nerve Resection, *M. Times, New York* **73**:315-316 (Nov.) 1945.

805. Lange, C., De: Dystonia Musculorum Progressiva (Torsion Dystonia), *Ann. paediat.* **164**:169-181, 1945.

806. Curman, H.: Dystonia Lenticularis (Double Athetosis, Torsion Spasm, Wilson's Pseudosclerosis), *Nord. med. (Hygiea)* **16**:3468-3471 (Dec.) 1942.

troublesome reflexes and spasticity, infection of the urinary tract and intractible pain.

Poer<sup>807</sup> outlines the treatment and rehabilitative program which has been developed for patients paralyzed as a result of injuries to the spinal cord sustained in World War II. 1. The phase of initial and early therapy includes treatment on the battlefield, transportation and early definitive treatment. Adequate nutrition is supplied, and suprapubic cystotomy is performed if the patient is not voiding. 2. The phase of corrective treatment begins on the patient's arrival at a neurologic surgery center, where all services concerned with the care of these patients are coordinated under a director. Malnutrition, decubitus ulcers and infection of the urinary tract are corrected; foreign bodies at the site of the injury are removed, and if intractible pain, troublesome reflexes and spasticity are present, appropriate neurosurgical procedures are carried out. Any associated injuries, such as fractures or open colostomy wounds, are also cared for. A well planned educational, recreational and prevocational training program is coordinated with the treatment. 3. The phase of ambulation and economic security begins on completion of phase 2. In this period any necessary reconstructive orthopedic measures, such as procedures to provide stabilization of joints or restoration of motion, are carried out. Exercises to strengthen the muscles of the trunk and upper extremities, training in the use of braces, crutches and special walking devices and vocational training are given. It is of interest that approximately 2,500 injuries to the spinal cord occurred in World War II among Army and Navy combat troops. The mortality rate fell from an all-time high of 95 per cent in the Balkan Wars to approximately 20 per cent in World War II.

E. C. Elkins,<sup>808</sup> in a lucid, brief discussion with an appended case report, describes the physical rehabilitation of a paraplegic patient, especially with regard to the reeducation of the muscles of the back, abdomen and upper extremities, the use of crutches and the type of crutch gait to be employed.

Covalt<sup>809</sup> outlines the comprehensive program being developed by the Veterans Administration for the rehabilitation of the veteran with a severe injury to the spinal cord.

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807. Poer, D. H.: Newer Concepts in Treatment of Paralyzed Patients Due to War-Time Injuries of Spinal Cord: Outline of Plan and Statistical Analysis, *Ann. Surg.* **123**:510-515 (April) 1946.

808. Elkins, E. C.: Physical Rehabilitation After Injury to Spinal Cord: Report of Case with Details of Procedures, *Proc. Staff Meet., Mayo Clin.* **21**:97-101 (March 6) 1946.

809. Covalt, D. A.: Rehabilitation of Veteran with Severe Spinal Cord Injury: Modern Medical Triumph! *Occup. Therapy* **25**:197-190 (Oct.) 1946.

Botterell and others<sup>810</sup> describe briefly the treatment of the paraplegic patient with a stable spinal column, including the management of the bladder, decubitus ulcers, pain and mass spinal reflexes. The braces which are of value in enabling these patients to walk are briefly discussed.

[ED. NOTE.—This paper outlines the problem concisely but contains insufficient detail about the various phases of treatment.]

Green<sup>811</sup> and Guttmann<sup>812</sup> also outline and discuss the care and rehabilitation of the paraplegic patient.

Harper<sup>812a</sup> discusses the care of paralyzed patients from the nutritional standpoint. Measures for correction of hypoproteinemia and vitamin deficiency, which are usually present in the paraplegic patient, are outlined, and it is pointed out that a sound nutritional plan must be included if the surgical and medical management of these patients is to be successful.

[ED. NOTE.—This discussion is excellent, though brief.]

According to C. W. Elkins and Wegner,<sup>813</sup> the most frequent neurosurgical problems in their experience in cases of paraplegia in World War II are those of retained foreign bodies in close proximity to the spinal cord or the peripheral nerve roots, intractable pain and uncontrolled spinal reflexes. Indications for removal of retained foreign bodies are: (1) intractable pain; (2) the presence of a foreign body either in, or in close approximation to, the cauda equina; (3) the presence of an intraspinal foreign body in any location (to prevent further formation of scar tissue), and (4) a persistent draining sinus. For the relief of pain, lysis of scar tissue may be indicated if the patient's condition will permit such a procedure. If the patient cannot tolerate such a procedure, spinothalamic chordotomy is effective. Subarachnoid spinal injections of alcohol are not advocated, because of the danger of upsetting an already precarious functioning of the bladder. Uncontrolled spinal reflexes vary in extent and degree, from simple flexion of a limb to the characteristic mass or spinal reflex. Conservative

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810. Botterell, E. H.; Jousee, A. T.; Aberhart, C., and Cluff, J. W.: Paraplegia Following War, *Canad. M. A. J.* **55**:249-259 (Sept.) 1946; *Cincinnati J. Med.* **27**:595-623 (Sept.) 1946.

811. Green, P.: Outline of Care of Paraplegic Patient, *Manitoba M. Rev.* **26**:506-509 (Sept.) 1946.

812. Guttmann, L.: Rehabilitation After Injuries to Spinal Cord and Cauda Equina, *Brit. J. Phys. Med.* **9**:130-137 (Sept.-Oct.) 1946.

812a. Harper, H. A.: Nutritional Aspects of Care of Paralyzed Patients, *Bull. U. S. Army M. Dept.* **5**:63-67 (Jan.) 1946.

813. Elkins, C. W., and Wegner, W. R.: Newer Concept in Treatment of Paralyzed Patient Due to War-Time Injuries of Spine: Neurosurgical Complications, *Ann. Surg.* **123**:516-522 (April) 1946.

treatment, consisting of splinting, bracing and physical therapy, should be employed early, with attention to the prevention of deformity. The administration of curare in moderate doses is helpful in conjunction with the other conservative measures. Later, if necessary, neurectomy of the nerve supply to the adductor muscles may be employed if there is a disabling "scissors" deformity of the legs, preventing walking with braces. If severe spasms of the flexors or extensor muscles persist in the patient with a complete lesion of the spinal cord, the anterior rhizotomy of Munro will produce flaccidity in the legs. Since a given reflex state is not necessarily fixed and some patients show a gradual reduction of the uncontrolled activity, even to partial flaccidity, radical neurosurgical procedures should not be employed early.

James and Braden<sup>814</sup> report the results of the use of curare in the treatment of 12 patients with paraplegia secondary to transverse myelitis, as the result of wounds. Dosage and precautions are discussed, and the authors note that spasticity diminished in every patient for one to two or more hours after every administration of an effective dose. The spasticity gradually returned to its original severity in from four to seven hours after injection; in no instance did the effects of a single administration of curare last more than twenty-four hours. The authors state the belief that the reduction of spasticity, though transient, was an aid in nursing care and physical therapy promoted healing and facilitated skin grafting of decubitus ulcers, and enabled patients to obtain rest at night; in 2 cases, for reasons unexplained, pain was relieved. The authors concur in the opinion of other writers that spastic muscles are affected by curarization with appreciably smaller doses than are innervated muscles.

Ward<sup>815</sup> presents a discussion of para-articular calcification, which may occur in the lower extremities of paraplegic patients. The calcification may be of major degree, though usually it is of minor degree about the knee. The author reports 4 cases, in 1 of which there was extensive para-articular calcification about the knees and one hip, the disorder in the hip being associated with fragmentation of the articular surface of the head of the femur. In discussing the cause of the calcification, it is brought out that the patients had massive edema of the lower extremities at some time after the injury, that the paralysis was usually complete and that there was rapid demineralization of the bones of the lower extremities, associated with hypercalciuria. Repeated minor traumas to the connective tissue structures, with degen-

814. James, D. F., and Braden, S.: Use of Curare in Treatment of Spastic Paralysis, *J. Neurosurg.* 3:74-80 (Jan.) 1946.

815. Ward, W. C.: Para-Articular Calcification in the Lower Extremities of Paraplegic Patients, *Am. J. Roentgenol.* 55:712-715 (Dec.) 1946; *Bull. U. S. Army M. Dept.* 6:771-776 (Dec.) 1946.



erative changes, may result in further attrition and in localized areas of hemorrhage, leading to calcification. Extensive areas of calcification may limit joint motion and interfere with the rehabilitation of the patient. Calcifications about the hip are especially subject to repeated traumas and may eventually become severe enough to limit motion, thus rendering sitting difficult. One patient sustained a fracture of the neck of the femur while turning in bed; when the fracture was recognized several weeks later, extensive calcification and deformity had developed, which prevented the patient from sitting up or beginning the use of braces for ambulation. No treatment is recommended for para-articular calcification or for extensive calcification of soft tissues. Fractures and chipping of articular surfaces may result from too vigorous efforts at rehabilitation.

[ED. NOTE.—This is an interesting paper on a complication seen rather infrequently in civilian practice.]

Emmett <sup>816</sup> describes urologic care in the case reported by Elkins.<sup>808</sup> The suprapubic cystotomy, which was present on the patient's admission, was allowed to close, and a transurethral resection was performed to relieve an obstruction of the vesical neck. After this procedure, vesical function was almost normal. The author describes the physiology of micturition and discusses the indications for transurethral resection in the treatment of disorders of the bladder in patients with paraplegia due to spinal injury.

Deery <sup>817</sup> reviews 23 consecutive cases of Pott's paraplegia in which laminectomy was performed because of failure to respond to conservative measures. Fifteen patients showed a manometric block, and 2 had no block but did have increased protein in the spinal fluid. Of these, 8 (of whom 5 were children) regained the ability to walk well, while 3 improved to the degree that they could walk with varying degrees of difficulty. Ten showed no improvement, and 2 died, 1 of tuberculous meningitis and 1 of generalized tuberculosis. The location for laminectomy was determined by the sensory level present. In all cases the locations of the sensory level, the intraspinal lesion and the apex of the kyphos corresponded very closely. Deery stresses that laminectomy is performed for decompression only, the intraspinal extradural abscesses being aspirated but peridural granulations and ventral compression of the cord by bony ridges being left strictly undisturbed. The laminectomy is made longer and wider than usual, both in those

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816. Emmett, J. L.: Transurethral Resection of the Vesical Neck in the Management of Cord Bladder, *Proc. Staff Meet., Mayo Clin.* **21**:102-107 (March 6) 1946.

817. Deery, E. M.: Laminectomy for Pott's Paraplegia, *Ann. Surg.* **124**:201-203 (Aug.) 1946.

cases in which fusion has previously been done and in those in which it is to be carried out at the time of laminectomy.

*Miscellaneous Neurologic Conditions Involving the Extremities.*—Gurdjian and Smathers<sup>818</sup> report a study of 53 cases of injury to peripheral nerves associated with fractures and dislocations of long bones for which operations were performed. The results are discussed, and pertinent papers are reviewed. Numerous drawings, depicting approaches and operative findings, accompany the paper.

Schwartz and Parker<sup>819</sup> relate their experience with early repair of the radial nerve and the humerus in persons with war wounds. They employed secondary débridement, with fixation of the fracture within a five to fourteen day interval after injury; the neurosurgical procedure was carried out three weeks or more after injury. In some cases, at the time of débridement and fixation of the bone, the nerve is approximated with a single silk suture and is surrounded by fibrin film, in order to prevent as much scarring about the nerve as possible until such time as nerve suture can be done. The authors are of the opinion that paralyzed nerves should be visualized at the time of definitive care of the fracture unless there is specific information from the forward hospital giving assurance that the nerve is intact. No end results are given.

In an excellent, fundamentally important paper, Thompson<sup>820</sup> discusses the problem of rehabilitation of the upper and lower extremities after irreparable peripheral nerve injury. The appropriate operative procedures, such as the various tendon transfers and joint stabilizations are discussed as to indications and technic.

Altman and Trott<sup>821</sup> report a modification of Billington's procedure for restoration of the extensor function of the hand and wrist in cases of irreparable lesions of the radial or the dorsal interosseous nerve. In an effort to avoid the sloughing at the angle of the Billington incision and persistent edema of the dorsum of the hand, the authors utilize multiple small incisions and attach the transferred flexor tendons into the extensor and thumb abductor tendons proximal to the dorsal carpal ligament. In most instances of complete paralysis of the radial nerve the tendons of the flexor carpi ulnaris and flexor carpi radialis and the pronator teres muscle are utilized as transfers. In cases of

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818. Gurdjian, E. S., and Smathers, H. M.: Peripheral Nerve Injury in Dislocations of Long Bones, Tr. West. S. A. (1944) 52:496-525, 1945.

819. Schwartz, H. G., and Parker, J. M.: Radial, Early Nerve and Bone Repair in War Wounds, J. Neurosurg. 2:510-515 (Nov.) 1945.

820. Thompson, T. C.: Orthopedic Measures for Use in Irreparable Nerve Injury, J. Internat. Coll. Surgeons 9:116-129 (Jan.-Feb.) 1946.

821. Altman, H., and Trott, R. G.: Wrist Drop: Muscle Transplantation for Paralysis of Radial Nerve, J. Bone & Joint Surg. 28:440-446 (July) 1946.

lesions of the dorsal interosseous nerve, the use of the pronator teres is not necessary. In some instances in this series the palmaris longus was transferred into the tendon of the abductor pullicis longus, as suggested by Bunnell. The authors report having used this procedure in 26 cases, with no failures.

[ED. NOTE.—No personal experience with this technic has been had by the reviewer.]

Pruce<sup>822</sup> describes a simple, easily made splint, designed to prevent the typical hyperextension of the metacarpophalangeal joint of the third and fourth fingers in paralysis of the ulnar nerve. It consists of a soft leather cuff, encircling the proximal phalanges of the third and fourth fingers, and is attached to a wristlet by a rubber band, with the line of pull toward the carpal navicular bone. The splint should be worn until recovery is complete or until it is determined that there is no hope of recovery.

Uflyand and Forshtadt<sup>823</sup> report on pseudoparalysis of the radial nerve due to inhibition of the nerve centers as a result of war wounds of the forearm.

Cannon and Love<sup>824</sup> report 38 cases of tardy palsy of the median nerve, with insidious onset and gradual impairment of function. In 9 of the cases in which operation was done, good results followed section of the transverse carpal ligament and neurolysis. In some patients severe neuritic pain is present, and occasionally trophic ulcers may be observed on the tips of the index and long fingers. This condition may follow a fracture of the wrist after a latent period of many years. The authors stress the importance of distinguishing such lesions of the wrist from lesions of the cervical portion of the spine, protruded cervical disks, the scalenus anticus and cervical rib syndrome, brachial plexus neuritis and progressive muscular atrophy. When the diagnosis is in doubt, roentgenograms of the wrist and cervical portion of the spine should be made routinely.

Jackson<sup>825</sup> has studied the role of galvanism in the treatment of denervated voluntary muscle in man, to determine the effective dose and frequency of treatment and whether any beneficial effect is produced. Ninety-two subjects were studied. She found that for a short period

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822. Pruce, A. M.: To Correct Deformity (Claw-Hand) Resulting from Injury to Ulnar Nerve, *J. Bone & Joint Surg.* **28**:397 (April) 1946.

823. Uflyand, Y. M., and Forshtadt, R. A.: Pseudoparalysis of the Radial Nerve Due to Inhibition of Nerve Centers Following War Wounds of the Forearm, *Byull. eksper. biol. i med.* **17**:21-23, 1944.

824. Cannon, B. W., and Love, J. G.: Tardy Median Palsy; Median Neuritis; Median Thenar Neuritis Amenable to Surgery, *Surgery* **20**:210-216 (Aug.) 1946.

825. Jackson, S.: Role of Galvanism in Treatment of Denervated Voluntary Muscle in Man, *Brain* **68**:300-330 (Dec.) 1945.

after denervation the volume of the part decreases whether or not galvanism is used; when no galvanism is used, wasting continues for about four hundred days and thereafter remains constant, whereas if galvanism is used the rate of wasting is decreased during the first one hundred days and the process ceases thereafter. Galvanism should be used as early as possible after denervation; there should be no break in the continuity of treatment, which should be continued in adequate intensity and frequency and with the effective number of contractions until sufficient voluntary control returns. Galvanism appears to be particularly valuable when immobilization is necessary, the period of denervation is long or the return of independent movements is poor. It is of less importance in children and very active youths.

Jones, LeCompte and Kabat <sup>826</sup> report the use of curare to differentiate the limitation of passive motion of the joints as a result of muscular spasm from that due to organic changes, including intra-articular and extra-articular ankylosis, whether partial or complete. The information is of value in prognosis as well as in outlining treatment. The results obtained in 17 cases are given, some in detail. The number of each of the various types of cases is small, and in some of the cases in which improvement in joint motion was noted after the use of curare the follow-up period is not of sufficient length.

[ED. NOTE.—This is a most interesting and valuable paper and should be of use in cases of this type, particularly from a differential diagnostic and prognostic standpoint.]

Hollingshead and Markee <sup>827</sup> report the results of a careful anatomic study of cadaver material in regard to multiple innervation of the individual muscles of the extremities. Markee and Löwenbach had previously demonstrated in dogs that multiple nerves entering a muscle may control the contraction of different segments of the muscle. In 1 carefully dissected human cadaver, of 58 separate heads of origin of the long muscles of the limbs all but 15 were entered by nerve branches at more than one point. Ten of these 15 muscles have been observed to receive more than one branch in other cadavers. The multiple branches may enter the muscle close together or may be distributed for some distance over the length of the muscle. Though the physiologic studies have not been carried out on human beings, observations on certain patients with partial paralysis indicate that the same

826. Jones, C. W.; LeCompte, C. B., and Kabat, H.: Studies on Neuromuscular Dysfunction: VIII. Use of Curare to Differentiate Muscle Spasm from Organic Changes in Limitation of Passive Motion at Joints, *South. M. J.* **39**:799-804 (Oct.) 1946.

827. Hollinshead, W. H., and Markee, J. E.: Multiple Innervation of Limb Muscles in Man, *J. Bone & Joint Surg.* **28**:721-731 (Oct.) 1946.

phenomenon of segmented contraction occurs. As an example, the authors state that the displacement of the bulge of a muscle on contraction, associated with weakness of the muscle (as seen in certain patients after poliomyelitis), is apparently due to unopposed contraction of a segment of the muscle and stretching of part of the muscle elsewhere.

[ED. NOTE.—This is a most interesting and valuable paper and should be read in its entirety.]

Caldwell and his associates<sup>828</sup> report their experiences with blocking of the stellate ganglion with procaine hydrochloride U. S. P. in a total of approximately 400 cases, comprising a variety of orthopedic conditions. From this number, 78 cases with adequate follow-up observations were studied. Briefly summarized, results were as follows: 1. In 88 per cent of 18 cases of acute subdeltoid bursitis, immediate relief was obtained, though in 50 per cent additional blocks were required, and in 16.7 per cent good results were obtained, though relief was not so dramatic. 2. In 12 cases of periarthrititis of the shoulder, the end results were not so striking, but pain was relieved sufficiently to make possible a much more active range of motion for the institution of physical therapy. 3. In 5 cases of myositis and fibrositis of a group of muscles, eventual relief was obtained over a longer period, probably owing to anesthetization of the communicating branches to the fifth and sixth cervical nerves from the middle cervical ganglion. 4. In 8 cases of hypertrophic arthritis of the shoulder, elbow or hand, only transitory relief was obtained, probably because of the irreversible tissue changes already present. 5. In the 5 cases of various types of infectious arthritides, as might have been expected, only temporary relief of pain was obtained. 6. In 17 cases of pain and swelling following fractures and dislocations, blocking of the stellate ganglion was done after reduction of the fractures and dislocations, with pronounced relief of pain and swelling. (The authors now use this procedure almost routinely for patients complaining of pain and tight casts; in many instances it is possible to avoid cutting casts which formerly would have required splitting.) 7. In 8 cases of pain and swelling after trauma (contusions), relief of pain was almost immediate. 8. In 8 cases of post-traumatic causalgia and "fantom pain" after amputation, blocking of the stellate ganglion gave excellent relief from pain and diminution of swelling. In some cases the blocking must be repeated at intervals. The authors describe the two technics that they employ, that of de Sousa Pereira and that of Patzer.

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828. Caldwell, G. A.; Borderick, T. F., Jr., and Rose, R. M.: Sympathetic Block of Stellate Ganglion: Application to Orthopedic Conditions, *J. Bone & Joint Surg.* 28:513-520 (July) 1946.

Ruskin<sup>829</sup> reports the spectacular relief in 63 cases of various conditions, such as "lumbosacral spasm (sacroiliac)," chronic and Marie-Strümpell arthritis and torticollis. This was achieved by anesthetization of the sphenopalatine ganglion, supplemented by administration of ferrous adenyate (ironyl®) and calcium ascorbate. The author states that the anesthetization of the ganglion is followed by immediate generalized relaxation of spasm of both smooth and striated muscle, as well as of cardiac muscle. He also advocates this treatment for coronary spasm, migraine, renal colic and dysmenorrhea.

[ED. NOTE.—The results reported in this paper should be verified.]

Schumacker<sup>830</sup> discusses the problems in surgical treatment of gangrene in cases of trench foot. Proper emphasis is placed on the value of lumbar sympathetic ganglionectomy in the treatment of the vasoconstriction. The author also discusses treatment of infection of the gangrenous part, amputations, skin grafting and plastic revision of stumps.

[ED. NOTE.—This is an excellent paper and should be read completely.]

Ulmer and Mayfield<sup>831</sup> present a valuable analysis of 75 cases of causalgia from the Percy Jones Hospital. In 88 per cent the injury was proximal to the knee and elbow, and in 60 per cent the burning pain developed within the first forty-eight hours. In all cases the nerve injury was incomplete. The vasomotor alterations were of two types: (1) vasodilatation, with reddish, dry, scaly, warm skin and long, coarse hair, and (2) vasoconstriction, with cold, thin, glistening skin, profuse sweating, loss of hair, tapering of the digits and trophic changes in the nails. Blocking with procaine hydrochloride of the appropriate sympathetic ganglions invariably gave immediate and dramatic relief for one to three hours, and in a few cases partial relief was present for several days; however, no patient obtained complete and permanent relief from the procedure, even when it was repeated. The authors are of the opinion that blocking of the sympathetic ganglions serves two purposes: First, by relieving the pain temporarily, it permits a more accurate evaluation of the nerve injury; second, it establishes the indication for sympathectomy. In the cases in which

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829. Ruskin, S. L.: Control of Muscle Spasm and Arthritic Pain Through Sympathetic Block at Nasal (Sphenopalatine) Ganglion and Use of the Adenylic Nucleotide (Ferrous Adenyate): Contributions to Physiology of Muscle Metabolism, *Am. J. Digest. Dis.* **13**:311-320 (Oct.) 1946.

830. Schumacker, H. B., Jr.: The Surgical Treatment of Gangrene in Trench Foot, *Surg., Gynec. & Obst.* **83**:513-520 (Oct.) 1946.

831. Ulmer, J. L., and Mayfield, F. H.: Causalgia: Study of Seventy-Five Cases, *Surg., Gynec. & Obst.* **83**:789-796 (Dec.) 1946.

they were employed, neurolysis and periarterial sympathectomy were of no benefit. The pain can be relieved by sympathectomy, which must be complete and must include the injured segment of the nerve; in cases of high sciatic lesions it may be necessary to remove the sympathetic chain as high as the eleventh dorsal ganglion. Ordinarily, the authors employ a preganglionic sympathectomy of the second and third dorsal ganglions in patients with lesions of the upper extremity and removal of the second, third and fourth lumbar ganglions in those with lesions of the lower extremity.

White<sup>832</sup> discusses painful injuries of the peripheral nerves, their surgical treatment and the probable underlying pathologic factors; this is followed with a lucid description of the types of pain, including the pain due to painful neuromas, that of causalgia and that of phantom limb. The various methods of treatment for pain are then considered, and the consensus of the various procedures is given. The following procedures are useless and should no longer be considered: (1) repeated resection of neuromas; (2) neuroclonic treatment or interruption of the nerve trunks at higher levels; (3) reamputation for relief of pain; (4) periarterial sympathectomy; (5) introthecal injections of alcohol and (6) posterior rhizotomy. On the other hand, a single resection of a sensitive neuroma is of distinct value, especially if the hyperesthesia is localized and can be relieved with local infiltration of procaine. Interruption of the sympathetic ganglionic chain, either by repeated chemical blockage with procaine or by sympathectomy, is of great value in patients with the vasomotor and emotional states so frequently noted in these painful conditions. Spinothalamic tractotomy is of value in relieving the pain and tenderness located within the stump itself but is not reliable in relieving phantom pain. Resection of the sensory cerebral cortex has been used successfully in the treatment of phantom limb but is too new a procedure to be completely evaluated. The final approach to the problem of unbearable pain of a phantom limb is the elimination of introspection and self-centered concentration on the condition, which naturally develop as a result of the persistent intractible pain, by the prefrontal leukotomy of Freeman and Watts. This procedure, like postcentral cortical resection, is as yet in the experimental stage and must be further evaluated. Obviously, these procedures are intended for use in cases of the severe and intractible pain in a phantom limb and are indicated as a last resort.

[ED. NOTE.—This, too, is an excellent paper and is deserving of close study.]

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832. White, J. C.: Painful Injuries of Nerves and Their Treatment, *Am. J. Surg.* 72:468-488 (Sept.) 1946.

Lhermitte and Mouzon<sup>833</sup> report a case in which a lesion of the sciatic nerve was followed by muscular hypertrophy and hyperplastic osseous dystrophy. Alajouanine, Thurel and Houdart<sup>834</sup> report and discuss a case of sciatic paralysis, complicated by an embolic infarction of the buttock and by causalgia, which followed the intragluteal injection of a bismuth salt.

Cole<sup>835</sup> reports 7 cases of maternal obstetric paralysis which occurred in a series of 45,000 deliveries at the woman's clinic of the New York Hospital. Characteristically, the condition exhibits a combination of the following factors: primiparity, prolonged labor, difficult delivery and cephalopelvic disproportion. The pelvis may show a short posterior ilium, a sacral ala with a shallow anterior concavity and a promontory which does not encroach on the posterior pelvic cavity. Clinically, pain during labor referred along the course of the sciatic nerve is the earliest sign and may be overlooked. As labor continues and contractions become more intense, the pain becomes severer and paresthesias may develop. At this time, paralysis and spasmodic contractions of the muscles may develop. In many cases, the condition may not be recognized for several days. The degree of paralysis varies, ranging from drop foot to extensive flaccid paralysis of both lower extremities; it is usually unilateral. The condition is due to trauma of the lumbosacral plexus by the fetal head or, less frequently, by instruments. Prevention depends on recognition of the signs of compression of the lumbosacral cord; a change in method of delivery, e. g., to cesarean section, may be considered. Treatment of the paralysis is conservative, consisting of support of the injured extremity, physical therapy, galvanic stimulation and protection with a brace. The prognosis is guarded, recovery occurring as early as seven to ten days after birth or paralysis clearing up very slowly and incompletely.

Edmunds and Fey<sup>836</sup> present a discussion of the serratus anticus syndrome (isolated paralysis due to neuritis of the long thoracic nerve), with characteristic winging of the scapula. The etiologic features, clinical manifestations and treatment are considered; 2 cases are reported. Passerini<sup>837</sup> reports 2 cases of this condition, while

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833. Lhermitte, J., and Mouzon, J.: Muscular Hypertrophy and Hyperplastic Osseous Dystrophy Following a Lesion of the Great Sciatic Nerve and Its Roots, *Rev. neurol.* **73**:606-608 (Nov.-Dec.) 1941.

834. Alajouanine, T.; Thurel, R., and Houdart, R.: Sciatic Paralysis with Causalgia Associated with Embolic Infarction of Buttock, Due to Intragluteal Injection of Bismuth Salt, *Rev. neurol.* **78**:58-60 (Jan.-Feb.) 1946.

835. Cole, J. T.: Maternal Obstetric Paralysis, *Am. J. Obst. & Gynec.* **52**:373-386 (Sept.) 1946.

836. Edmunds, L. H., and Fey, L. D.: Serratus Anticus Syndrome, *Clin. Virginia Mason Hosp.* **24**:49-52 (June) 1946.

837. Passerini, L.: Report of Two Cases of Paralysis of the Serratus Magnus, *Rassegna previd. sociale* **12**:10-15 (Dec.) 1940.



Lindqvist<sup>838</sup> reports an instance of this condition due to working with a pneumatic drill.

Desirotte<sup>839</sup> discusses "operation table" paralysis, due to faulty positioning of the unconscious patient on the operating table. Unusual positions which may be assumed in association with complete muscular relaxation may result in tension or stretch of the nerves of the brachial plexus. Proper attention to positioning, with adequate precaution, can prevent this complication.

[ED. NOTE.—American readers should again study the paper of Clausen.<sup>840</sup>]

Eaton,<sup>841</sup> in a well written paper, discusses the neurologic causes of pain in the upper extremities. He calls attention to the difficulty and importance of differentiating between neurologic lesions and non-neurologic lesions which give rise to referred pain, such as that from the viscera and the deep-lying somatic structures. The intramedullary lesions of the central nervous system which may give rise to pain in the upper extremities are most frequently syringomyelia and intramedullary tumor of the spinal cord. Root pain may result from rheumatoid spondylitis, hypertrophic spondylitis, ruptured intervertebral disks or extramedullary tumors of the spinal cord. Eaton points out that there are three characteristics of root pain which are of great diagnostic significance: 1. The distribution of the pain is within the segment supplied by a particular nerve root. 2. The pain is frequently intensified by coughing, sneezing and straining; this is the result of increased intraspinal pressure, resulting from blockage of the flow from the intervertebral veins by the increased intrathoracic and intra-abdominal pressure. Engorgement of the veins of the epidural spaces thus occurs, and this, in turn, either produces pressure on the nerve root directly or stretches the root by displacing the dura toward the spinal cord. 3. The root pain is intensified by stretching of the involved nerve roots. The diagnosis of a ruptured cervical disk is then discussed. Among the syndromes due to lesions of the brachial plexus are those of mechanical compression, including the cervical rib syndrome, the scalenus anticus syndrome, the subcoracoid pectoralis minor syndrome of Wright, the costoclavicular syndrome of Falconer and Weddell and the first thoracic rib syndrome. Nocturnal dyses-

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838. Lindqvist, T.: Case of Paralysis of the Serratus Anterior Due to Work with the Pneumatic Drill, *Nord. med. (Hygiea)* **26**:1163-1164 (June 1) 1945.

839. Desirotte, A.: So-Called "Operation Table" Paralysis, *Rev. méd., Liège* **1**:101-102 (Aug. 15) 1946.

840. Clausen, E. G.: Postoperative ("Anesthetic") Paralysis of the Brachial Plexus: Review of Literature and Report of Nine Cases, *Surgery* **12**:933-942 (Dec.) 1942.

841. Eaton, L. M.: Neurologic Causes of Pain in the Upper Extremities, *S. Clin. North America* **26**:810-833 (Aug.) 1946.

thesia, traumatic lesions of the brachial plexus, tumors, inflammatory lesions and serum neuritis are also considered. Lesions of the peripheral nerves are briefly discussed.

[ED. NOTE.—This paper should be read in *toto* by all orthopedic surgeons.]

Paull<sup>842</sup> reports a case of Wright's subcoracoid pectoralis minor syndrome which was successfully treated by conservative measures, including change of sleeping habits and stretching and reeducation of muscles.

In a paper discussing the results of conservative treatment in a series of cases of "sciatic neuritis," as compared with an analogous series of cases in which a diagnosis of ruptured intervertebral disk had been confirmed by operation, Dunning<sup>843</sup> states that the prognosis for recovery was satisfactory in 54 per cent of the cases of sciatic neuritis, while operation in the cases of ruptured intervertebral disk promptly relieved the pain and bettered the prognosis by 32 per cent. However, it is Dunning's opinion that natural processes should be given an opportunity to repair the defect before spinal operation is urged. The neurologic signs and the protein content of the spinal fluid were not found to be of prognostic value. The author maintains that the symptoms and signs of a ruptured intervertebral disk in the fourth or fifth lumbar intervertebral space are indistinguishable from the well defined syndrome formerly called sciatic neuritis.

Mack<sup>844</sup> reports a case of meralgia paresthetica in which, at the time of operation, it was noted that the lower fibers of the inguinal ligament exerted a compressive and shutter-like action on the lateral femoral cutaneous nerve in its passage over the brim of the pelvis. This, he feels, may be the underlying etiologic factor. He prefers the operation described by Lee for this condition. Graber-Duvernay<sup>845</sup> also reports on meralgia paresthetica.

*Ocular Torticollis.*—Kennedy<sup>846</sup> reports the case of a 57 year old woman who had "drawing of the neck" of twelve years' duration. It was first thought that she had a spasmodic type of torticollis, and the usual orthopedic measures were used, without relief. Later, it was found that she had a crossed and vertical diplopia, as a result of paralysis

842. Paull, R.: The Neurovascular Syndrome as Manifested in the Upper Extremities, *Am. Heart J.* **32**:32-38 (July) 1946.

843. Dunning, H. S.: Prognosis in So-Called Sciatic Neuritis, *Arch. Neurol. & Psychiat.* **55**:573-577 (June) 1946.

844. Mack, E. W.: Meralgia Paresthetica: New Causal Observations, *West. J. Surg.* **54**:390-391 (Oct.) 1946.

845. Graber-Duvernay, J.: Remarks on Femorocutaneous Neuralgia (Meralgia Paresthetica) Observed at the Center for Displaced Persons in Aix-les-Bains, *Rev. du rhum.* **13**:97-99 (April) 1946.

846. Kennedy, R. J.: Ocular Torticollis: Report of a Case, *Cleveland Clin. Quart.* **13**:163-165, 1946.

of the superior rectus muscle on the side of the head tilt, with overaction of the inferior oblique muscle on the opposite side. The differential diagnosis is as follows:

#### Ocular Torticollis

1. Head tilt not pronounced
2. Sternocleidomastoid muscle not actually contracted; slight "tightness" of structures on side of tilt
3. Head passively straightened, but binocular vision interrupted; diplopia present unless patient "fixes" with one eye only and neglects the image of the other
4. Face usually rotated slightly toward side of head tilt; in some cases turned downward
5. Abnormal conjugate ocular movements present
6. Extraocular muscular imbalance present

#### Spasmodic Torticollis

1. Obvious head tilt
2. Gross contracture of sternocleidomastoid muscle on side of tilt
3. Head tilt cannot be passively corrected
4. Face always rotated away from side of head tilt and turned upward
5. Conjugate ocular movements normal
6. Extraocular muscular balance normal

The treatment of ocular torticollis consists primarily of shortening or advancing of the affected muscle, orthoptic training and the use of prisms, if necessary. In cases of long standing, when there is apparent hypertrophy of the sternocleidomastoid muscle, an intradural section of the anterior (motor) nerve roots of the first three cervical nerves bilaterally and a section of the spinal accessory nerve on the affected side are indicated.

*Degenerative Diseases.*—Wechsler and Brody<sup>847</sup> consider the problem of primary lateral sclerosis and its relation to the other scleroses of the spinal cord. They are of the opinion that it is a distinct clinical syndrome, unrelated to the other scleroses. The scleroses are all merely the result of the selective affinity of various endogenous and exogenous noxious agents for specific structures of the nervous system. Neither multiple sclerosis nor amyotrophic lateral sclerosis presents a single etiologic or pathologic entity; each consists of several syndromes, in fairly consistent clinical groups. The authors note that there appears to be an increase in incidence of the more benign types of these degenerative diseases of the nervous system, so that, despite want of knowledge of causes, one may venture a less hopeless prognosis.

Gordon,<sup>848</sup> in an interesting paper, adds 2 pure, or unmixed, cases of primary lateral sclerosis to the literature; these have been followed by him for twenty-four years. He is of the opinion that "subacute degeneration" has a legitimate place in the variety of forms of primary lateral sclerosis, in which there is an absence of spasticity of the

847. Wechsler, I. S., and Brody, S.: Problem of Primary Lateral Sclerosis, *J. A. M. A.* **130**:1195-1198 (April 27) 1946.

848. Gordon, A.: Clinical Status of Unmixed Types of Primary Latéral Sclerosis After Twenty-Four Years of Observation (Subacute Degeneration), *J. Nerv. & Ment. Dis.* **103**:378-382 (April) 1946.

musculature of the extremities from the onset and an absence of contracture throughout the course of the disease.

Simmons,<sup>849</sup> in an article dealing with his experiences with curare as an adjunct to general anesthesia and in the treatment of spastic paralysis, reports favorable results in 2 cases of disseminated sclerosis with parkinsonism and in 1 case of "degenerative and idiopathic" Parkinson's disease.

[ED. NOTE.—Because of the small series reported the results are inconclusive.]

Halpern<sup>850</sup> reports a posterior spinal syndrome characterized by (1) sensory ataxia of the legs and (2) loss of vibratory sense in segmental distribution, the remainder of the nervous system is intact. The loss of vibratory sense was located in the sacral and lumbar segments. In all cases the condition cleared up within six weeks. There was no paresis, atrophy or disturbed reflexes in any of the patients; no pain was present on pressure over the nerve trunks or muscles. Halpern reports 6 cases of this condition, which he considers a primary involvement of the posterior portion of the spinal cord, involving the tract of Goll.

Lipson and DeNardi<sup>851</sup> report and discuss 3 cases of Friedreich's ataxia.

DeGennaro<sup>852</sup> discusses the complications and sequelae of syringomyelia, including secondary deformities.

Campailla<sup>853</sup> reports a case of syringomyelobulbia following peripheral trauma of the thigh.

Nosik<sup>854</sup> reports a case of olivopontocerebellar atrophy (heredocerebellar ataxia of Marie) with encephalographic findings.

Planson<sup>855</sup> reports on cases of familial spastic paraplegia.

849. Simmons, H. J. A.: Preliminary Investigation of the Use of Curare in Anesthetic Practice and for Treatment of Spastic Paralysis, *Brit. J. Anaesth.* **20**:34-38 (Jan.) 1946.

850. Halpern, L.: Ataxia of Legs and Loss of Vibration: Isolated Spinal Syndrome, *J. Nerv. & Ment. Dis.* **104**:474-479 (Nov.) 1946.

851. Lipson, H. A., and DeNardi, J. M.: Friedreich's Ataxia (A Familial Hereditary Study of Three Cases), *Dis. Nerv. System* **7**:261-267 (Sept.) 1946.

852. DeGennaro, R.: The Deformities Following Syringomyelia, *Clinica, Bologna* **10**:120-131, 1945-1946.

853. Campailla, G.: Syringomyelobulbia Syndrome Following Peripheral Trauma of the Thigh, *Gior. med. mil.* **93**:311-319 (July-Aug.) 1946.

854. Nosik, W. A.: Olivopontocerebellar Atrophy (Heredocerebellar Ataxia of Marie) with Encephalographic Findings: Report of a Case, *Cleveland Clin. Quart.* **13**:203-207 (Oct.) 1946.

855. Planson: Familial Spastic Paraplegia, *Paris méd.* **1**:105-108 (March 9) 1946.

In a detailed study, Charcot-Marie-Tooth disease and the other heredodegenerative diseases are discussed and cases reported by Bancalari Rodriguez.<sup>856</sup>

*The Myopathies.*—Freeman<sup>857</sup> reports the postmortem findings in 4 cases of amyotonia congenita. The muscles showed the usual paleness and thinness, with underdevelopment. In the nervous system, the ventral roots were thin, pinkish and translucent, while the dorsal nerve roots appeared normal. The brain itself was grossly normal. Microscopic examination of the spinal cord showed a great reduction in the number of the ventral horn cells at all levels, with no indication of degeneration or reaction. The myelin sheaths of the fiber tracts of the spinal cord were small and irregularly grouped. The brain showed thinning of the precentral cortex, with less numerous cellular elements, especially the giant multipolar cells of Betz, which were also abnormal in size and shape. The cortex was immature in regard to cellular arrangement, with a tendency to column orientation. No degenerated cells were seen; rather, they were of an immature type. Some cellular deficiency, though to a less degree, was noted in the postcentral convolutions. Freeman concludes that amyotonia congenita appears to be a disorder in which there is a defective development of the whole motor system, from the precentral gyrus to the muscles. It has its counterpart in amyotrophic lateral sclerosis, in which there is degeneration of the whole motor system from the precentral cortex to the muscles.

Hanhart<sup>858</sup> reports a study of 29 cases of infantile spinal muscular atrophy (Werdnig-Hoffman syndrome) which occurred as simple recessive sublethal mutations in fourteen families.

Matus<sup>859</sup> points out that the primary myopathies, unlike the secondary muscular atrophies, have no apparent neural lesion as a cause. The former all have these distinguishing etiologic and clinical characteristics: 1. They occur in infants and adolescents. 2. They often take on a familial aspect, sometimes being hereditary. 3. The muscles, during the period of atrophy, do not present fibrillary contractions; the small tremors of the muscle fascicles, visible through the skin in patients with myelopathic atrophy, are here conspicuous by their absence. 4.

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856. Bancalari Rodriguez, E.: Progressive Amyotrophy of Charcot-Marie-Tooth: A Contribution to the Study of Heredodegenerative Diseases, *Rev. neuropsychiat.* 8:488-546 (Dec.) 1945.

857. Freeman, W.: The Motor Cortex in Amyotonia Congenita, *J. Neuropath. & Exper. Neurol.* 5:207-212 (July) 1946.

858. Hanhart, E.: Infantile Progressive Spinal Muscular Atrophy Occurring as a Simple Recessive, Sublethal Mutation, *Helvet. paediat. acta* 1:110-133 (Nov.) 1945.

859. Matus, S.: Primary Myopathy Characterized by "Micropygia" in the First Generation and Scapulohumeral Dystrophy in the Second One of Consanguineous Parents, *South African M. J.* 20:170-171 (April 13) 1946.

Reaction of degeneration is absent, very early changes in chronaxia indicating a mixture of healthy fibers and pathologic fibers in the affected muscles. 5. The atrophy begins in the big muscles of the shoulder, arm, back and thigh, rather than in the small muscles of the hand. 6. The distribution of the muscular atrophy, once established, is characteristic, the muscles of the distal parts of the extremities being respected while disappearance of the muscles of the thighs and the lumbar region results in a special attitude of the patient and causes deformities. 7. Sometimes the muscles of the face are involved in the progressive atrophy. 8. The muscular atrophy is sometimes accompanied with considerable adiposity of the lower limbs, giving a false appearance of muscular hypertrophy (pseudohypertrophy). 9. The reflexes are not exaggerated, there being no disorder of bulbar origin, such as an accelerated pulse or paralysis of the palate.

Four types of primary myopathies are described: (1) Leyden-Möbius dystrophy; (2) juvenile type (Erb); (3) Landouzy-Dejerine atrophy and (4) pseudohypertrophic type. However, these types cannot be separated into definite groups. The author reports 2 cases, of brothers aged 5 and 6, of the pure scapulohumeral type of atrophy. The father showed micropygia (small buttocks), with fatty adiposity overlying the upper part of the gluteus muscles. He stated that his cousin (his father's brother's daughter) had the same condition. Also, his wife was a cousin, the daughter of another of the father's brothers.

In a paper devoted to differentiation of the primary myopathies, such as progressive muscular dystrophy of the distal, or Gowers', type and the secondary myopathies, such as progressive muscular atrophy, Bowden and Gutmann,<sup>860</sup> of Oxford University, report detailed multiple biopsies in 2 cases. They conclude that advanced atrophy in the muscle fibers, intact large intramuscular nerve trunks and abortive terminal regeneration of the nerve fibers are characteristic features of the muscles in a case of progressive muscular dystrophy, while in the so-called secondary myopathies, such as peroneal muscular atrophy, the nerve trunks may be empty or may contain both normal fibers and empty Schwann tubes; occasionally, they may contain regenerated nerve fibers. The authors advocate muscle biopsy as an aid to diagnosis in unusual cases of muscular atrophy and weakness.

Hafner and others<sup>861</sup> report the results in 9 cases of progressive muscular dystrophy in which treatment was with synthetic *d,l*-alpha-tocopherol acetate (ephynal acetate<sup>®</sup>), for periods of three to twenty-

860. Bowden, R. E. M., and Gutmann, E.: Observations in a Case of Muscular Dystrophy, with Reference to Diagnostic Significance, *Arch. Neurol. & Psychiat.* 56:1-10 (July) 1946.

861. Hafner, P. G.; Anderson, R.; Davis, H., and Chuinard, E. G.: Treatment of Progressive Muscular Dystrophy with Synthetic Di-Alpha-Tocopherol, *North-west Med.* 45:256-258 (April) 1946.

seven months. Four patients showed objective increase in the strength of certain muscle groups, as well as subjective improvement; 2 remained in the same condition, and 3 gradually became weaker, despite treatment. No changes were noted in the urinary excretion of creatine or creatinine. Garces Cuadra and Montes R<sup>862</sup> report their results in the therapy of progressive muscular dystrophy, utilizing alpha-tocopherol.

Fagin<sup>863</sup> reviews the clinical features of dystrophia myotonica and presents 2 cases. One case was that of a female patient with diabetes mellitus and a colloid goiter, suggesting that endocrinopathy may be an important factor, while the second was that of a male patient, with an associated hyperostosis frontalis interna. The author brings out that the latter condition (also known as metabolic craniopathy) is a syndrome with endocrine, metabolic and neurologic changes associated with alterations in the bony structure of the skull and appears to be closely related to pituitary dysfunction.

Weinberg-Heyrouti and Reif<sup>864</sup> report a case of acute dermatomyositis in a child.

*Neurogenic arthropathy.*—Delano<sup>865</sup> discusses the history of the theories of the etiology and pathogenesis of Charcot's joint. After examining the evidence, the author notes that there is no definite proof of the existence of "trophic" nerves and states the belief that the changes in neurogenic arthropathy are brought about by the occurrence of repeated minor subclinical traumas in an insensitive joint.

Smith<sup>866</sup> describes the osseous changes which may occur in yaws, these ordinarily being not unlike the low grade type of osteomyelitis of the long bones, which becomes quiescent of its own accord. In the spine, erosions, spurs and bony bridges may appear, often closely resembling the changes in hypertrophic arthritis. Patients usually have relatively little pain in proportion to the extensiveness of the bone changes. The author reports a case of yaws in a native of the Marshall Islands, whose bilateral involvement of the knee and ankle was clinically identical to the typical manifestation of Charcot's joint in late syphilis.

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862. Garces Cuadra, H., and Montes R, O.: Alpha-Tocopherol Therapy for Progressive Muscular Dystrophy, *Rev. chilena de pediat.* **16**:798-811 (Aug.) 1945.

863. Fagin, I. D.: *Dystrophia Myotonica: Report of Two Cases with Associated Hyperostosis Frontalis Interna in One*, *J. Michigan M. Soc.* **45**:500-503 (April) 1946.

864. Weinberg-Heyrouti, C., and Reif, L.: Acute Dermatomyositis in a Child, *Ann. paediat.* **166**:193-202, 1946; addendum, *ibid.* **167**:215, 1946.

865. Delano, P. J.: Pathogenesis of Charcot's Joint, *Am. J. Roentgenol.* **56**:189-200 (Aug.) 1946.

866. Smith, F. H.: Charcot-Like Joints in Yaws, *U. S. Nav. M. Bull.* **46**:1832-1843 (Dec.) 1946.

## ACUTE ABDOMINAL MANIFESTATIONS IN SICKLE CELL DISEASE

A Report of Three Cases, with Laparotomy in Two

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ONLY a small proportion of Negroes with the sickle cell trait have the active form of the disease.<sup>1</sup> In 1929 Levy<sup>2</sup> found that of 213 Negroes admitted in succession to the New Rochelle Hospital, 12, or 5.8 per cent, had "sickling." Murphy and Shapiro<sup>3</sup> recorded its incidence in the North American Negro as from 7 to 13 per cent, with anywhere from 1 in 7 to 1 in 40 of those affected showing clinical disease and with a total of almost 135,000 diseased in the United States. Wintrobe<sup>4</sup> expressed the belief that 1 in 40 Negroes in North America and up to 9 per cent in Central and South America are so affected.

Huck<sup>5</sup> first pointed out that the trait was transmitted by the male and the female as a mendelian dominant characteristic. It occurs in males in a ratio of 3 to 1<sup>6</sup>; usually children and adolescents are affected, though persons up to 78 have shown evidence of the disease. It has been reported in white persons,<sup>4</sup> and in 1 case involving a 19 year old American-born white youth it was followed by laparotomy.<sup>7</sup>

The abdominal manifestations of sickle cell disease are generally recognized to be as much a part of it as the pains in the bones, joints and muscles or the leg ulcers, but their cause remains obscure. The

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1. Campbell, E. H.: Acute Abdominal Pain in Sickle Cell Anemia, *Arch. Surg.* **31**:607-621 (Oct.) 1935.

2. Levy, J.: Sicklemia, *Ann. Int. Med.* **3**:47-54 (July) 1929.

3. Murphy, R. C., Jr., and Shapiro, S.: The Pathology of Sickle Cell Disease, *Ann. Int. Med.* **23**:376-397 (Sept.) 1945.

4. Wintrobe, M. M.: *Clinical Hematology*, Philadelphia, Lea & Febiger, 1946, p. 501.

5. Huck, J. G.: Sickle Cell Anemia, *Bull. Johns Hopkins Hosp.* **34**: 1923, cited by Steinberg.<sup>6</sup>

6. Steinberg, B.: Sickle Cell Anemia, *Arch. Path.* **9**:876-897 (April) 1930.

7. Canby, C. B.; Carpenter, G., and Ellmore, L. F.: Drepanocytosis (Sicklemia) and an Apparently Acute Surgical Condition of the Abdomen: Report of Their Occurrence in a White Youth, with Laparotomy, *Arch. Surg.* **48**:123-125 (Feb.) 1944.



pains may be gradual, vague and generalized in onset or acute, excruciating and prostrating. They are usually unaccompanied with changes in abdominal muscle tone, but this is not necessarily the case. Prostrating epigastric pain associated with nausea and vomiting, rigidity, generalized tenderness and rebound may herald the onset of a crisis and be so difficult to differentiate from an acute abdominal condition requiring surgical treatment as to make operation advisable and even mandatory, with occasional catastrophic consequences.<sup>8</sup> Operation has been performed in 2 cases which we shall later present in detail.

#### THE CAUSES OF ABDOMINAL DISTRESS IN SICKLE CELL CRISIS

The cause of abdominal distress in sicklelemlia is an important and interesting controversial problem. Yater and Mollari<sup>9</sup> in 1931 suggested arterial thrombosis as one of the causes. In 1932 Leivy and Schnabel<sup>10</sup> pointed out that the pains resemble those of root origin, that they are neurogenic and find their cause in vertebral changes as a result of marrow hyperplasia, with compression of the bodies and pressure on the nerve roots. Campbell<sup>1</sup> in 1935 reported 6 cases, in 3 of which exploration gave negative results. All of the patients recovered. He pointed out that many of these patients have abdominal pain at some time and that this pain may simulate any kind of intra-abdominal visceral disorder. He believed one of the causes to be splenitis and perisplenitis, but this is not borne out by the cases of Leivy and Schnabel<sup>10</sup> or of Landon and Patterson.<sup>11</sup> Sydenstricker, Mulhern and Houseal<sup>12</sup> believed splenic hemorrhage to be a cause of the pain, while Cooley<sup>13</sup> ascribed abdominal crisis to splenic thrombosis.

Tomlinson<sup>8a</sup> reported on 11 patients, all of whom died and were examined at autopsy. Six of a total of 13 patients examined at autopsy

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8. (a) Tomlinson, W. J.: Abdominal Crises in Uncomplicated Sickle Cell Anemia: A Clinico-Pathologic Study of Eleven Cases with a Suggested Explanation of Their Cause, *Am. J. Med. Sc.* **209**:722-741 (June) 1945. (b) Bauer, J.: Sickle Cell Disease, Pathogenic, Clinical and Therapeutic Considerations, *Arch. Surg.* **41**:1344-1362 (Dec.) 1940. Footnotes 1, 2 and 4.

9. Yater, W. M., and Mollari, M.: The Pathology of Sickle Cell Anemia: Report of a Case with Death During an Abdominal Crisis, *J. A. M. A.* **96**:1671-1675 (May) 1931.

10. Leivy, F. E., and Schnabel, T. G.: Abdominal Crises in Sickle Cell Anemia, *Am. J. Med. Sc.* **183**:381-391 (May) 1932.

11. Landon, J. F., and Patterson, H. A.: An Evaluation of Splenectomy in the Treatment of Sickle Cell Anemia: Late Results of Two Cases So Treated with a Summary of the Present Condition of All Splenectomized Patients, *J. Pediat.* **7**:472-477 (Oct.) 1935.

12. Sydenstricker, V. P.; Mulhern, W. A., and Houseal, R. W.: Sickle Cell Anemia: Report of Two Cases in Children, with Necropsy in One Case, *Am. J. Dis. Child.* **26**:132-154 (Aug.) 1923.

13. Cooley, T. B.: Indications for Splenectomy in Childhood, *Journal-Lancet* **54**:673-676 (Nov. 1) 1934; cited by Landon and Patterson.<sup>11</sup>

showed chronic hepatitis, 6 of 9 patients with abdominal crisis who died had palpable lymph nodes, 9 of 11 had fatty changes in the liver, all displayed enlargement and softening of the intestinal lymph nodes with fibrosis of the spleen and 6 had perisplenitis. The lymph nodes showed "marked hyperplasia of the reticuloendothelial cells with extensive phagocytosis of sickled erythrocytes." There was likewise marked edema of the stroma and of the endothelial cells lining the sinuses. Tomlinson summed up the clinical picture as follows:

. . . the sudden onset of distress or pain in the abdomen usually accompanied by nausea and vomiting; rigidity or tenderness in the abdomen with occasionally pain or tenderness in the muscles or bones of the extremities not involving the joints; malaise, severe chill followed by fever, most frequently jaundice, early rather rapid peripheral vascular collapse with tachycardia, weak pulse, hyperpnea and signs of central nervous system involvement.

Patients with these symptoms, he believed, die in shock, which is secondary to sickling from anoxia, packing of capillaries by deformed red blood cells, loss of plasma and hemoconcentration.

Murphy and Shapiro<sup>8</sup> stated the opinion that the pains were due to vascular occlusion following thrombosis. Hemolytic crisis is initiated by an accumulation of circulating sickle cells, with an increased tendency toward sickling as the patients grow older. These cells then precipitate out in a "simultaneous capillary blockade" and cause a crisis. They expressed the opinion that the one factor initiating the mechanism is an altered state of coagulability resulting from the increased quantities of thrombin and thromboplastin liberated after multiple repeated small infarctions.

Josephs,<sup>14</sup> in searching for the cause of the hemolytic anemia, decided that the red cells absorb an unknown substance common to plasma, which alters the surface tension but can be washed off with isotonic sodium chloride solution. Normal red cells will not do this. Robinson<sup>15</sup> ascribed the cause of the hemolytic anemia to a hyperplasia or over-activity of the cells of the reticuloendothelial system.

Bauer<sup>8b</sup> wrote that the hemolysis was caused by "mechanical impaction of masses of deformed red blood cells in the smaller blood vessels in various organs." He says: "This impaction with the subsequent hemolysis of the resulting conglutinated masses is responsible for the further pathologic changes and for the clinical symptoms of sickle cell anemia." He believed sicklemia to be due to an inborn, constitutional, transmitted abnormality of erythropoiesis and that the sickle cell trait

14. Josephs, H. W.: Clinical Aspects of Sickle Cell Anemia, *Bull. Johns Hopkins Hosp.* **43**:397-399 (Dec.) 1928; **40**:77-84 (Feb.) 1927, cited by Yater and Mollari.<sup>9</sup>

15. Robinson, H. A.: Sickle Cell Anemia: Etiology, with Report of a Case, *J. Michigan M. Soc.* **34**:388-393 (June) 1935.

represents one of the congenital stigmas associated with other congenital abnormalities. Thrombosis, ischemia, necrosis and fibrosis follow the destruction of red blood cells. Anoxemia, infection, surgical procedures and other factors slowing the circulation can initiate the whole vicious cycle of events. He reports on 1 patient with sickle cell anemia who, after a compatible transfusion, had a reaction and died. Autopsy showed an enlarged liver and a tremendous mediastinal, tracheobronchial and abdominal lymphadenopathy caused by increase in reticular tissue. Sydenstricker, Mulhern and Houseal<sup>12</sup> reported hyperplasia of the mesenteric lymph nodes among other findings at necropsy in a patient who before death had complained of pain high in the abdomen.

Since 1938 we have treated 23 patients with sickle cell disease at this hospital. It is of interest to us that 8, or 34 per cent, complained chiefly of symptoms that were predominantly and recurrently gastrointestinal in nature. In this group 13 were females and 10 males, the age ranging from 1 month to 50 years<sup>10</sup> and averaging 12 years. The longest duration of symptoms was seventeen years. In many of these patients a crisis would begin with vague generalized abdominal pains or discomfort, the prodromal symptoms becoming typical of a relapse. In a considerable number of cases symptoms referable to the cardiovascular system were noted and frequently rheumatic fever suspected. This is easily understood in view of the associated arthralgia, prostration, fever, pain in the chest, hemic murmurs and borderline electrocardiographic findings, with roentgenologic evidence of enlargement of the heart to the right and left.

Three of the patients died. J. C. is reported on in some detail later. R. W., a woman aged 50, died of intestinal obstruction secondary to a Meckel diverticulum, and autopsy revealed splenomegaly and fibrosis of the liver and spleen, with cirrhosis of the liver. At postmortem examination M. C. showed dilatation and hypertrophy of the right side of the heart and the left auricle, dilatation of the pulmonary conus, hepatomegaly with central necrosis and engorgement of the sinusoids and periportal fibrosis with marked disease of the mesenteric lymph glands, which microscopically showed disorganization and increase in macrophages. The spleen was contracted, fibrotic, hyalinized and calcified. The cause of death was failure of the right side of the heart.

In 2 instances abdominal exploration was performed. One of the patients recovered after a stormy course in the hospital, and only after operation was it determined that he was suffering from a crisis in sickle cell anemia. Two sisters and a brother were found to be similarly affected, with a record of previous admissions to this hospital

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16. Cohen, S. M.; Miller, B. W., and Orris, H. W.: Fatal Sickle Cell Anemia in a One Month Old Infant, *J. Pediat.* **30**:468-472 (April) 1947.

for relapses. In the other patient, a 1 month old infant known to have the disease, death occurred soon after operation. This patient was moribund when operated on. In a third case a diagnosis of acute appendicitis had been made. Operation was averted when the mother informed us that the child had sickle cell anemia and took her home. She had previously been treated in other institutions for similar complaints.

#### PRESENTATION OF CASES

CASE 1.—J. C.,<sup>16</sup> a 1 month old Puerto Rican female infant, was admitted to the hospital on July 9, 1946, with the chief complaint of fever, anorexia and irritability of one day's duration. The temperature was 104 F., the white blood cell count was 13,200, with 36 per cent polymorphonuclear cells and 64 per cent lymphocytes, and the hemoglobin content was 11.5 Gm. Urinalysis showed 3 red cells and 3 white cells per high power field. On July 9 it was noted that the child was icteric. The icterus index at that time was 130, with an immediate direct van den Bergh reaction, a serum protein content of 6.3 Gm. per hundred cubic centimeters and a cephalin flocculation reaction of 1 plus. Hematologic analysis showed a leukocyte count of 26,500, with a hematocrit value of 23 and two nucleated red blood cells per hundred white cells. There was normochromic anemia, and red cells showed anisocytosis and poikilocytosis, with occasional target cells; no spherocytosis was noted. Bleeding and clotting times were normal; the blood type was O, Rh positive. The child was given a transfusion of 50 cc. of whole blood and, because of the otitis media, placed on penicillin therapy. Two days later, wet preparation of the blood showed sickling of the red cells. There were no cold agglutinins present, and puncture of the tibial bone marrow gave negative results. On the seventh day, despite apparent improvement, the red blood cell count was 1,240,000 and the hemoglobin content 5.5 Gm., and for the following week neither showed much change.

One week later the icterus had increased. The child began vomiting and had diarrhea, was observed to moan constantly and appeared sicker. Sickling was again reported from examination of the wet preparation. At this time a mass was felt in the right upper quadrant, extending from below the liver to the umbilicus, and some abdominal distention was noted. That evening the child was markedly dyspneic. The skin was ecchymotic and mottled over the mass and the abdomen markedly distended, and a diagnosis of intussusception was made. After supportive treatment, and at the insistence of the pediatricians, laparotomy was performed and disclosed only moderately severe mesenteric adenitis. The child died four hours after operation.

Postmortem examination revealed hemorrhagic cystitis, metritis, pyelitis, renal hypertrophy with infarction and hemorrhage, hemorrhagic esophagitis and gastritis, bilateral bronchopneumonia, splenomegaly and lymphoid hyperplasia of the nodes and intestinal follicles. The small intestine was distended and contained numerous small areas of subserosal hemorrhage; there were multiple areas of superficial and deep hemorrhagic infarctions of the brain and a congenital stricture of the right ureteropelvic junction. There was an epidural hemorrhage as a result of transfusion into the sagittal sinus.

CASE 2.—S. C., a 20 year old Negro, was admitted on April 13, 1947, with a complaint of excruciating, generalized abdominal pain of four hours' duration, most marked in the lower quadrants. Bowel movements on the preceding day had

been normal, without blood, and though he had had previous attacks of abdominal pain due to what he termed indigestion, none had been as severe as this one. The past history was not suggestive of peptic ulcer.

Examination disclosed a thin, well nourished Negro writhing in pain. Physical abnormalities were confined to the abdomen, where there was boardlike rigidity and direct and rebound tenderness throughout. Roentgenologic examination of the abdomen showed an air bubble under the left hemidiaphragm, interpreted as free air. The white blood cell count was 14,700, with 89 per cent polymorphonuclear cells and 11 per cent lymphocytes. Urinalysis revealed nothing remarkable.

Shortly after his admission the patient was operated on for a ruptured peptic ulcer through a right subcostal muscle-splitting incision. The peritoneum was found free of pathologic changes except for markedly enlarged mesenteric, retroperitoneal and common duct lymph nodes. The liver was enlarged 3 to 4 finger-breadths below the costal margin and was pale and dull, with evidence of chronic hepatitis. The stomach and duodenum were thoroughly explored, the lesser omental sac entered and the pancreas examined, and all were found to be normal. The gallbladder and the biliary tract were then manually and visually examined, and they too were found free of pathologic changes. The foramen of Winslow was almost occluded by enlarged lymph nodes in the hepatic pedicle. The wound was closed, and the patient returned to the ward in critical condition. He was treated with gastric suction, intravenous administration of fluids, oxygen, sodium sulfadiazine and large doses of penicillin. On the following day, an examination of the blood by the laboratory showed notable sickling of the red blood cells at the end of thirty minutes and twenty-four hours, with a total red blood cell count of 1,500,000, a hemoglobin content of 8.5 Gm. and 11 normoblasts per hundred white blood cells. The red cells showed anisocytosis and poikilocytosis, and a diagnosis of crisis in sickle cell anemia was made.

The past history revealed that the patient had been hospitalized for hepatitis while in the navy. A summary of his course in the naval hospital revealed that on April 13, 1946, he was admitted with a diagnosis of infectious hepatitis, confirmed by laboratory findings of hepatic insufficiency. Blood studies at that time were not remarkable, and no wet preparations had been examined. Liver function tests were regularly repeated until October 1946, when the reactions were found to be normal and he was discharged for duty.

Hematologic survey of other members of his family at this time revealed that 2 sisters and 1 brother had the sickling abnormality.

His further course in our hospital was uneventful until the fifth postoperative day, when he had a severe reaction to a transfusion of 250 cc. of matched whole blood. He responded rapidly to supportive treatment, and on the nineteenth day after his admission he was discharged to the outpatient department for follow-up care.

CASE 3.—V. R., an 8 year old Negro girl, was admitted to the hospital on Oct. 7, 1943, with a complaint of sudden onset of periumbilical pain which was sharp, recurrent and unrelieved by nausea and vomiting. Examination showed an acutely ill patient. There was slight abdominal distention, with spasticity throughout, and deep tenderness, but no rebound, was present in the right lower quadrant and periumbilically. There was no palpable mass or viscus. The white blood cell count was 25,000, with 81 per cent polymorphonuclear cells, 3 per cent stab cells, 1 per cent eosinophils and 15 per cent lymphocytes. The chest and the urine were normal, and a diagnosis of acute appendicitis was made.

While awaiting the consent of the mother to operation, we were notified that the child had been known to have sickle cell anemia for the past five years and had suffered previous similar attacks. Operation was postponed, and the child was later taken home by her mother.

#### COMMENT

We should like to postulate as one of the causes of abdominal pain in sickle cell crisis a mesenteric and retroperitoneal lymphadenitis and lymphadenopathy, noted in each of the 2 patients examined and at autopsy in 2 others and previously noted.<sup>17</sup> Whether this is the result of intercurrent infection of the upper respiratory tract, as may well have been the case in regard to our first patient (J. C.), or whether it is part of the picture of reticular hyperplasia so frequently noted in the abdominal lymph nodes of these persons in crisis is difficult to say. Hematopoiesis has also been suggested as a cause. It is understandable that this frequently noted lymphadenopathy may give rise to pain, as does the mesenteric adenitis following an infection of the upper respiratory tract, when the nodes are inflamed and swollen. We believe further that thrombotic episodes, coexistent hepatitis and hepatosis, splenitis and perisplenitis may be secondary causes. The frequency of hepatic dysfunction associated with the disease has been previously noted.<sup>18</sup> Many cases are characterized by positive cephalin flocculation reactions, and pathologic changes in the liver are repeatedly noted at operation and autopsy. Lowe and Adams<sup>18a</sup> ascribed the hepatomegaly to stagnation of sickle cells in the hepatic sinusoids, with increased phagocytic activity of the Kupffer cells, parenchymal edema and degeneration. Stasney<sup>18b</sup> found the liver to be enlarged, red, brown and firm. There was congestion, distention of the sinusoids and swelling of the Kupffer cells associated with erythrophagocytosis and hemosiderosis. Ryerson and Terplan<sup>18c</sup> described a case in which a diagnosis of subacute liver atrophy was confirmed when autopsy was performed, and Dale<sup>18d</sup> mentioned 2 more.

We were interested in utilizing the recently developed Winsor-Burch parameter test<sup>19</sup> for the diagnosis of sickle cell anemia, and in

17. Syndenstricker and others.<sup>12</sup> Robinson.<sup>15</sup> Bauer.<sup>8b</sup>

18. (a) Lowe, R. C., and Adams, C. C.: Studies on the Pathophysiology of Sickle Cell Disease, *Ann. Int. Med.* **22**:192-200 (Feb.) 1945. (b) Stasney, J.: Erythrophagocytosis and Hemosiderosis in the Liver and Spleen in Sickle Cell Disease, *Am. J. Path.* **19**:225-237 (March) 1943. (c) Ryerson, C. S., and Terplan, K. C.: Sickle Cell Anemia: Two Unusual Cases with Autopsy, *Folia hæmat.* **53**:353-369, 1935; cited by Bauer.<sup>8b</sup> (d) Dale, G. C.: Sickle Cell Anemia, *South. Med. & Surg.* **99**:14-16 (Jan.) 1937, cited by Bauer.<sup>8b</sup> Levy.<sup>2</sup>

19. (a) Winsor, T., and Burch, G. E.: Sickle Cell Anemia, "A Great Masquerader," Easily Recognizable with Routine Use of Diagnostic Parameter, *J. A. M. A.* **129**:793-796 (Nov.) 1945; (b) Diagnostic Pysiochemical Blood Tests in Sickle Cell Anemia, *Am. J. M. Sc.* **207**:152-160 (Feb.) 1944.

our last patient the reaction was decidedly positive on two occasions, to the extent where differences in sedimentation rates between anoxic and well oxygenated blood was 47 mm. per hour in the first determination and 92 mm. per hour in the second. We used the aeration-tourniquet technic.

#### SUMMARY

The crisis in sickle cell disease must be considered in the differential diagnosis of an acute abdominal condition requiring surgical treatment if unnecessary laparotomy is to be avoided.

The abdominal distress seen in sickle cell crisis is undoubtedly due to one or more of several factors, including mesenteric lymphadenopathy, splenic and hepatic thrombosis, vascular occlusions in the tissues of the abdominal wall, hepatitis and hepatosis and possibly neurogenic factors resulting from rarefaction of vertebral bodies with pressure on the roots.

We concur with Bauer<sup>8b</sup> and with Winsor and Burch<sup>19a</sup> in the belief that all Negroes deserve a routine examination of the wet preparation of the blood on their admission to the hospital to rule out sickle cell anemia when there is any question of the diagnosis of an abdominal condition requiring surgical treatment. This is hardly of less importance than a routine blood count. Certainly when the familial and past histories suggest the presence of the disease or when icterus, hepatomegaly or abdominal pain is noted, the hanging drop preparation should be examined for sickling.

We have presented 3 patients in whom the manifestations of sickle cell crisis were largely abdominal and in 2 of whom laparotomy was performed.

# ECHINOCOCCAL CYSTS OBSTRUCTING THE COMMON BILE DUCT

Report of Case

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**E**CHINOCOCCAL or hydatid cysts, especially in the liver, may attain great size without the production of prominent symptoms. It has been estimated that about 25 per cent of human beings infested with echinococci go through life without any symptoms or complaints referable to them.<sup>1</sup> In most cases, however, symptoms do appear, and often these are bizarre. It is the purpose of this paper to review some of the literature on echinococcal cysts which have caused obstruction of the common bile duct, to report data on 40 cases in which the diagnosis of primary echinococcal cysts of the liver was made and proved at the Mayo Clinic and to report an illustrative case in which a hydatid cyst ruptured into the biliary tract and gave rise to symptoms indicative of stone in the common duct.

About 70 per cent of primary echinococcal cysts are found in the liver and four of every five echinococcal cysts of the liver are in the right lobe.<sup>2</sup> Such a cyst may continue to grow for many years or for the life of the person affected without producing any signs except enlargement of the liver and the accompanying subjective symptoms, such as a sensation of weight or dragging in the upper part of the abdomen. More rarely symptoms of pressure, such as nausea, vomiting, jaundice, respiratory distress and even cardiac embarrassment may occur. A cyst of the liver may suppurate and then produce the clinical picture of hepatic abscess. The cyst may rupture into a large bile duct, with

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From the Division of Surgery, Mayo Clinic.

1. Napier, L. E.: Hydatid Disease, in the Principles and Practice of Tropical Medicine, New York, The Macmillan Company, 1946, pp. 737-746.

2. Barnett, L.: Hydatid Cysts: Their Location in the Various Organs and Tissues of the Body, Australian & New Zealand J. Surg. **12**:240-248 (April) 1943.



the production of biliary colic, into the peritoneal cavity, into the lung, pleura or bronchus or into a kidney, with the production of renal colic.

The association of jaundice with echinococcal cysts of the liver was first noted by Neisser<sup>3</sup> in 1877. Since then many studies of this condition have been made. However, few reports have appeared in North American literature. It should be noted that jaundice is rarely caused by direct compression of the bile ducts by an enlarging cyst. More often jaundice is due to embolic obstruction of the ducts by mother or daughter cysts, by portions of the cyst wall or by other debris coming from the mother cyst. Jaundice is then accompanied with colicky pain in the right upper part of the abdomen, and this syndrome has been referred to as "pseudolithiasis."<sup>4</sup>

Even more dangerous to the patient than the biliary obstruction is the suppuration in the mother cyst which is likely to ensue after intra-biliary rupture. This is the most common cause of suppuration within the primary cyst, and in some series rupture has been found in all cases in which suppuration occurred. The evacuation of the cyst and its walls into the biliary tract is not usually complete, but at times it may be, and spontaneous cure may result. Mason and Barnett<sup>5</sup> reported the passage of a complete thin-walled mother cyst through the bile ducts of a child. Jaundice and such severe colic were associated that exploratory operation was carried out. The patient subsequently vomited a ruptured cyst the size of a small tangerine. Duprey<sup>6</sup> claimed that 24 per cent of the patients are cured by drainage of the cyst through the bile ducts. An even higher percentage of cures were reported in cases in which the echinococcal cysts of the lung had spontaneously ruptured into a bronchus.

"Pseudolithiasis" is not an easy condition to diagnose. It is frequently missed even at exploratory operation. A dilated common duct is found, but there is no other evidence of gallstones. Subsequently, portions of the cyst may appear in drainage from the bile ducts. Even in regions in which the disease is relatively common a correct pre-operative diagnosis is made in less than 50 per cent of the cases.<sup>1</sup>

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3. Neisser, cited by Gennaro, J. F.: Echinococcus Cyst of the Liver Simulating a Stone in the Common Bile Duct, *J. Internat. Coll. Surgeons*. **3**:342-350 (Aug.) 1940.

4. Reyes, M., and Derqui, M.: Quiste calcificado de hígado a forma pseudolitiásica, *Bol. y trab., Soc. de cir. de Buenos Aires* **21**:768-774 (Sept. 15) 1937.

5. Mason, A. J., and Barnett, L.: Spontaneous Evacuation of a Hydatid Cyst of the Liver by Way of the Bile Ducts, *Australian & New Zealand J. Surg.* **7**:78-80 (July) 1937.

6. Duprey, G., cited by Dévé,<sup>10</sup>

There are several points of special note in establishing the diagnosis. About 95 per cent of the persons who have hydatid cysts in North America are immigrants, especially those from Italy, Iceland, Greece and Germany.<sup>7</sup> However, the incidence of the disease in its classic home, Iceland, has been greatly reduced.<sup>8</sup> The patients who have intrabiliary rupture of their cysts are usually younger than those who have cholelithiasis. The incidence of intrabiliary rupture of echinococcal cysts among males and females is about equal. The skin tests and the complement fixation test for echinococcosis are relatively simple to perform and are reliable. The greatest difficulty involved is the acquisition of fluid from a hydatid cyst for use as the antigen. The eosinophilia, which was great in the case which we are reporting, is suggestive of the diagnosis, but this is found in less than 25 per cent of patients with echinococcosis. With intrabiliary rupture of a cyst, hydatid material may be found in the stools, in vomitus or in material obtained by duodenal aspiration. Such a finding is of great value in establishing the diagnosis.

Dew<sup>9</sup> stated that some degree of intrabiliary rupture is the commonest complication of echinococcal cysts of the liver. Dévé,<sup>10</sup> however, regarded intraperitoneal rupture as the most frequent complication and gave the figure for intrabiliary rupture as only from 5 to 10 per cent of all hepatic hydatid cysts. The incidence of rupture into the bile ducts appears to be much greater in the cases in which the diagnosis has been made at the Mayo Clinic.

The case records of all patients seen at the clinic whose condition was diagnosed as echinococcosis were studied. The liver of 40 of these patients was proved to be the site of the primary cyst. Such proof was based on a combination of history, positive reaction to the skin test, clinical findings and anteroposterior and lateral roentgenographic views of the region of the liver or on the finding of a hydatid cyst at the time of operation. Application of these criteria caused us to exclude many probable cases of hydatid cysts of the liver. Of the 40 patients, 14 (35 per cent) gave a definite history of severe biliary

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7. Magath, T. B.: Hydatid Disease (Echinococcus) in North America, Pennsylvania M. J. **44**:813-819 (April) 1941.

8. Ofeigsson, O. J.: Hydatid Disease in Iceland, Proc. Staff Meet., Mayo Clin. **12**:420-421 (July 7) 1937.

9. Dew, H. R.: Hepatic Cysts Involving the Biliary Passages, in Hydatid Disease; Its Pathology, Diagnosis and Treatment, Sydney, The Australian Medical Publishing Company, Ltd., 1928, pp. 168-181.

10. Dévé, F.: Echinococcose hépatique (kystes hydatiques du foie), in Roger, G. H.; Vidal, F., and Teissier, P. J.: Nouveau traité de médecine, Paris, Masson & Cie, 1928, vol. 16, pp. 775-805.

colic at some time during the course of their disease. Thirteen of the 14 also gave a history of jaundice during some of their attacks of biliary pain.

All 14 patients were operated on. The patient who did not have jaundice was found to have gallstones and a moderate-sized hydatid cyst of the liver. It is interesting to speculate on the origin of the gallstones in this case, as to whether or not they may have arisen from a nidus of debris from a hydatid cyst.

Another 10 of the 40 patients (25 per cent) gave a history of mild or indefinite pain in the right upper abdominal quadrant during the period of their illness. Dew<sup>9</sup> stated that he was convinced that practically all the so-called painful types of apparently uncomplicated hydatid cysts of the liver are in reality due to minor ruptures, with passage of small pieces of debris or membrane into the ducts. He considered that this is a more likely explanation for the pain than hepatoptosis, pressure on the ducts, visceral distention or pressure on the celiac plexus.

The remaining 16 patients (40 per cent), although they had primary echinococcal cysts of the liver, either had no complaints referable to the biliary tract or had such vague complaints as bloating, indigestion or nausea and vomiting.

#### REPORT OF A CASE

The patient, an itinerant Greek immigrant 54 years old, had been seen at the clinic on ten previous occasions. He had been treated for latent syphilis, recurring gonorrheal urethritis, traumatic paralysis of the right opponens pollicis muscle, chemical burn of the conjunctiva, presbyopia and ecthymatous ulcers. In 1936, when he was seen at the clinic for the first time, a cholecystogram was made because of the complaint of pain in the right upper quadrant of the abdomen. It was found that the gallbladder functioned normally, but multiple areas of calcification were noted which, in lateral views, were shown to be in the liver. Reactions to the Casoni intradermal test and the complement fixation test with fluid from a hydatid cyst as antigen were both strongly positive. Blood smears disclosed an eosinophil content of 15.5 per cent. A diagnosis of calcified echinococcal cysts of the liver was made.<sup>11</sup> Because of the positive results of serologic tests for syphilis (Kline test grade 4 and Kahn test grade 4 on a grading basis of 1 to 4, reaction to Hinton test negative and Wassermann reaction strongly positive), operation was postponed for one month while antisyphilitic treatment was started. At the end of the month the patient had improved greatly and refused operation.

In June 1947, eleven years later, the patient returned to the clinic and was hospitalized for emergency treatment. The following history was obtained: Thirteen days previously severe, cramping, intermittent pain had begun gradually in the right upper quadrant of the abdomen and had continued for three days.

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11. Smith, H. L., and Magath, T. B.: Calcified Echinococcus Cysts in the Liver: Report of Case, Proc. Staff Meet., Mayo Clin. 12:405-408 (June 30) 1937.

This pain was superimposed on a dull, severe, constant pain of the right upper abdominal quadrant which had commenced at the time of the crampy pain and continued until the present admission. Morphine given by his physician had produced only temporary relief. The pain extended through the back, to the right axilla and across the chest to the left axilla. Vomiting had occurred at the onset but had ceased after two days. Jaundice had not been noted by the patient, but he had noticed that since the second day of the attack his urine had been dark and his stools light in color. There was no pruritus. Anorexia and chilly sensations had been present early in the illness but had subsided. For two years he had had episodes of dull precordial tightness which lasted about one hour. This was unrelated to exertion. He reported three previous episodes similar to his presenting complaints, one in 1936, one in 1937 which lasted about one hour, and one in 1946 which lasted three or four hours. Although the pain was similar in these episodes, he recalled no signs of jaundice.

On admission the patient appeared acutely ill and was moaning at intervals. Icterus was pronounced. The systolic blood pressure was 100 mm. of mercury and the diastolic 62 mm. The pulse rate was 84 and the temperature 99.8 F. There was some guarding in the right upper quadrant of the abdomen and pronounced but poorly localized tenderness in the region of the gallbladder. The liver was palpable down to 6 cm. below the right costal margin. No hydatid thrill was noted. The remainder of the history and physical examination was noncontributory.

The laboratory findings were reported as follows: The urine had a specific gravity of 1.010 and contained a moderate amount of albumin and a small amount of pus. There was 16 Gm. of hemoglobin per hundred cubic centimeters of blood. The erythrocytes numbered 5,500,000 and the leukocytes 9,800 per cubic millimeter of blood. There was an eosinophil content of 34 per cent. The Kline, Kahn, Hinton and Kolmer tests all gave negative results. The value for serum bilirubin was 6.6 mg. direct and 2.4 mg. indirect per hundred cubic centimeters. The prothrombin time (Quick) was 21 seconds, and the cephalin-cholesterol test gave negative results. The value for total cholesterol was 254 mg. and cholesterol esters 102 mg. per hundred cubic centimeters of plasma. The blood urea was 32 mg. per hundred cubic centimeters, and the sedimentation rate (Westergren) was 24 mm. per hour. The plasma protein content was 7 Gm. per hundred cubic centimeters. The stools were acholic. An electrocardiogram showed a slurred QRS complex in lead III and positive T waves in leads CR<sub>2</sub> and CR<sub>3</sub>. Roentgenograms of the thorax showed nothing remarkable, and one of the upper part of the abdomen revealed evidence of a large cystic lesion with calcification of its walls in the right lobe of the liver. The colloidal gold curve of the spinal fluid was 0111100000.

Four days after the patient's admission to the hospital the stools were still acholic, but on the fifth day duodenal drainage yielded dark green bile, the stools became greenish colored and the value for serum bilirubin fell slightly to 6.3 mg. direct and 0.9 mg. indirect.

Twelve days after the patient was admitted, on July 3, 1947, operation was performed by one of us (W. W.) through an upper right rectus incision. A large echinococcal cyst approximately 10 cm. in diameter occupied the right lobe of the liver. Half of this cyst projected from the lower portion of the right lobe and was calcified in places. The cyst was opened. The daughter cysts were removed, and the cyst was unroofed. A double strip of plain gauze was placed in the cyst cavity, as was a rubber tube for the introduction of solution of

formaldehyde. No stones could be felt in the gallbladder, but the wall was thickened and somewhat edematous. No stones could be felt in the common bile duct, which was dilated to about twice normal size. The gallbladder was opened, and no stones were found; a dressed tube was then placed in the gallbladder. The common bile duct was opened and black tarry bile with cholesterin crystals drained out. Three echinococcal cysts, each about 1.5 cm. in diameter, were removed from the common bile duct. Scoops were then passed through the lower end of the duct into the duodenum without encountering obstruction. Exploration of the intrahepatic ducts disclosed nothing. The head of the pancreas was enlarged to about twice normal size; this enlargement appeared to be due to pancreatitis. A T tube was placed in the common bile duct, and four Penrose drains were placed in the abdomen, which was then closed. The pathologist verified the surgical findings; many of the daughter cysts showed numerous scolices with horny hooklets.

The postoperative course was rather stormy. At no time was the patient in any danger, but he suffered from numerous pains and a temperature up to 103 F. on the third, fourth and fifth postoperative days. The cystic cavity in the liver was irrigated on the second, third and fourth days with a 2 per cent solution of formaldehyde. The patient's temperature was normal for the first time on the fourteenth day. The T tube was clamped for longer periods each day. A cholangiogram taken on the seventeenth day showed that the common duct was normal in size. The contrast medium entered the duodenum freely. The T tube was then removed.

The hepatic cyst was irrigated on alternate days with solutions of penicillin and streptomycin. Three months after operation there had been no appreciable change in the size of the cyst. The general condition of the patient, however, was excellent. He had gained weight, was free of jaundice, had no pain and had a good appetite. He was then dismissed from observation at the clinic. At the time of writing, seven months after operation, efforts to contact him were unsuccessful.

#### SUMMARY

In the case reported daughter echinococcal cysts had caused obstruction of the common duct. The clinical records of 40 patients who had proved primary hydatid cysts of the liver were studied. Fourteen of these patients (35 per cent) gave a definite history of severe biliary colic. Thirteen of the 14 had been jaundiced. Ten (25 per cent) gave a history of mild or indefinite pain in the right upper quadrant during the period of their illness. Sixteen (40 per cent) had no complaints referable to the biliary tract, although they had primary hepatic cysts.

## CHRONIC CHOLECYSTITIS PRODUCED BY DIVISION OF THE SPHINCTER OF ODDI

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**I**N AN EARLIER communication<sup>1</sup> it was shown that division of the sphincter of Oddi of dogs was followed by the appearance of diastase in the bile obtained from cholecystostomy tubes placed in such dogs. Normally, bile contains no diastase or negligible amounts of it. The effects of a prolonged reflux of duodenal contents into the gallbladder were obscured by the irritative effect of the cholecystostomy tube.

The present experiments were designed to determine (1) whether section of the sphincter of Oddi is followed by reflux of duodenal contents into the gallbladder when the latter is not decompressed by a cannula and (2) what the effects are of prolonged duodenal reflex through an incompetent sphincter of Oddi.

Observations relating to these problems have been described by Colp, Doubilet and Gerber.<sup>2</sup> These authors divided the sphincteric mechanism of the common duct of 3 dogs by inserting a specially designed sphincterotome through an opening in the gallbladder and thence through the common duct. The opening into the gallbladder was closed with a purse string suture. After eight, thirty and one hundred and fifty days the dogs were killed. The gallbladder of the dog sacrificed after eight days showed an acute inflammation. In the other 2 dogs there were acute and chronic inflammatory changes in the wall of the gallbladder. Further observations have been made by Mallet-

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From the Laboratory and Department of Surgery of the Jewish Hospital of St. Louis, and the Department of Surgery, Washington University School of Medicine.

1. Gray, S. H.; Heifetz, C. J.; Probststein, J. G., and Russi, S.: Effect of Division of Sphincter of Oddi on Bile Diastase of Dog, *Arch. Surg.* **47**:160 (Aug.) 1943.

2. Colp, R.; Doubilet, H., and Gerber, I. E.: Endocholedochal Section of Sphincter of Oddi, *Arch. Surg.* **33**:696 (Oct.) 1936.

Guy and his co-workers,<sup>3</sup> who transected the sphincter of Oddi of 8 dogs, employing a transduodenal approach. These dogs were observed for periods of eighty-three to three hundred and seventeen days. A marked inflammatory reaction in the wall of the common duct and chronic cholecystitis were observed when the dogs were killed. Precipitation of calculi was noted in 4 cases. In another paper Mallet-Guy and Auger<sup>4</sup> found that less histologic changes in the gallbladder developed in a dog which was subjected to a pyloric exclusion procedure as well as section of the sphincter of Oddi than in 2 other dogs subjected to division of the sphincter of Oddi alone.

#### EXPERIMENT

Ten normal, apparently healthy mongrel dogs were anesthetized with sodium pentobarbital, given intravenously. The abdomen was entered through an upper midline incision. The gallbladder was aspirated and the bile obtained was analyzed for diastase<sup>5</sup> provided it was not blood tinged. The opening of the common duct into the duodenum was exposed transduodenally. With one blade of a scissors inserted into the duct opening and the other on the duodenal mucosa, the duct was opened along its intramural course for a distance of about 1 cm. It should be noted that the procedure employed results in division of both components of the sphincter mechanism at the termination of the common duct, the sphincter of Oddi proper and the duodenal musculature which compresses the intramural portion of the duct. In this paper the term "sphincter of Oddi" is used to refer to the entire sphincter mechanism. Occasionally the same effect was secured by inserting a small curved hemostat into the opening of the ampulla and then cutting down on the slightly opened forceps tips with a small scalpel blade. The duodenum was then closed with one layer of fine intestinal sutures. The abdominal wall was closed in layers with nonabsorbable sutures.

At intervals ranging from four to eighty-six weeks after this initial operation the dogs were again anesthetized. The gallbladders were aspirated and the diastase concentration in the bile determined. Pieces of liver, pancreas, gallbladder and common duct were removed for microscopic study and the dog killed.

#### RESULTS

Only 2 of the 10 specimens of bile obtained at the time of the initial operation were considered suitable for diastase determination. These

3. Mallet-Guy, P.; Auger, L., and Billa, M.: *Compt. rend Soc. de biol.* **112**:899, 1933.

4. Mallet-Guy, P., and Auger, L.: *Lyons Chir.* **29**:629, 1932.

5. Somogyi, M.: *J. Biol. Chem.* **125**:399, 1938.

contained 0 and 150 units respectively. This last value is slightly higher than any previously reported by Gray, Probst and Heifetz but is still negligible in comparison with the amount of diastase in a dog's blood.

The diastase activity of the gallbladder bile obtained at the second operation, weeks after the division of the sphincter of Oddi, is given in the accompanying table. Grossly, the gallbladders all appeared normal at the time of the initial operation.

The anatomic and histologic observations are given in detail in the following paragraphs.

*Dog 20.*—This dog was killed four weeks after division of the sphincter. The opening of the common duct into the duodenum was wide. The gallbladder and the extrahepatic biliary ducts appeared normal. Sections of the gallbladder showed a chronic inflammatory reaction consisting of round cells and plasma cell infiltration, with some edema.

*Diastase Activity of the Gallbladder Bile*

Dog	Weeks from Operation to Day Killed	Preoperative Concentration of Diastase, Units	Postoperative Concentration of Diastase, Units
20.....	4	...	131
18.....	4	...	125
15.....	8	150	1,420
11.....	12	...	0
10.....	16	...	...
8.....	20	...	4,700
4.....	24	0	Insufficient quantity*
6.....	30	...	240
21.....	36	...	Insufficient quantity
22.....	39	...	770

\* The gallbladder contained matted hair, and bile could not be aspirated.

The serosa of the gallbladder was somewhat thickened. The sections of liver showed no inflammatory changes.

*Dog 18.*—This dog was killed four weeks after division of the sphincter. Grossly the gallbladder, liver and extrahepatic ducts appeared normal. In sections of the gallbladder there was dilatation of the subserosal lymphatic vessels. Section of the liver showed collections of large mononuclear cells, among which were a few plasma cells in the portal triads.

*Dog 15.*—This dog was killed eight weeks after division of the sphincter. At necropsy the gallbladder appeared thickened. The common duct was much thickened, particularly in the distal 2 cm. The entrance of the common duct into the duodenum was wide open. When the gallbladder was examined it was found to contain eight tan-colored concretions, each measuring 0.5 by 1 cm. Microscopic sections of the gallbladder showed the wall to be three or four times the normal thickness, owing primarily to edema in the muscularis and the submucosal



layers. The subserosal lymphatic vessels were dilated. There was a minimal infiltration of round cells into the muscularis and subserosa. Section of the liver showed no inflammatory reaction. The common duct epithelium was thrown into folds. There was a slight increase in connective tissue about the duct. The concretions were analyzed by Dr. M. Somogyi and reported to be almost entirely of calcium phosphate.

*Dog 11.*—This dog was killed twelve weeks after division of the sphincter. Grossly and microscopically the liver and the gallbladder appeared normal.



Fig. 1.—Section of liver of dog 8, killed twenty weeks after division of sphincter of Oddi, showing suppurative cholangitis.

*Dog 10.*—This dog was killed sixteen weeks after division of the sphincter of Oddi. At necropsy the opening of the common duct into the duodenum appeared essentially the same as it was before the sphincter was cut. The gallbladder, liver and common duct appeared normal grossly. Microscopic sections showed a normal gallbladder, liver and common duct.

*Dog 8.*—Dog 8 was killed twenty weeks after the division of the sphincter of Oddi. This dog was delivered of pups one month before she was killed. At necropsy the gallbladder and common duct appeared



Fig. 2.—Normal gallbladder of a dog.



Fig. 3.—Gallbladder of dog 4 six months after division of sphincter of Oddi. (Same magnification as in figure 2).

thickened. The ampulla was wide open. Microscopic sections showed a markedly thickened gallbladder wall. All layers were increased in depth. The muscularis was hypertrophied, somewhat edematous and infiltrated with lymphocytes. The subserosa was thick and consisted of old connective tissue. There was a large number of mitotic figures in the mucosal cells. Sections of the liver showed acute hepatitis, with abscess formation. The portal spaces were infiltrated with polymorphonuclear cells (fig. 1). Sections of the common duct showed an increased amount of connective tissue about the ducts. The epithelium

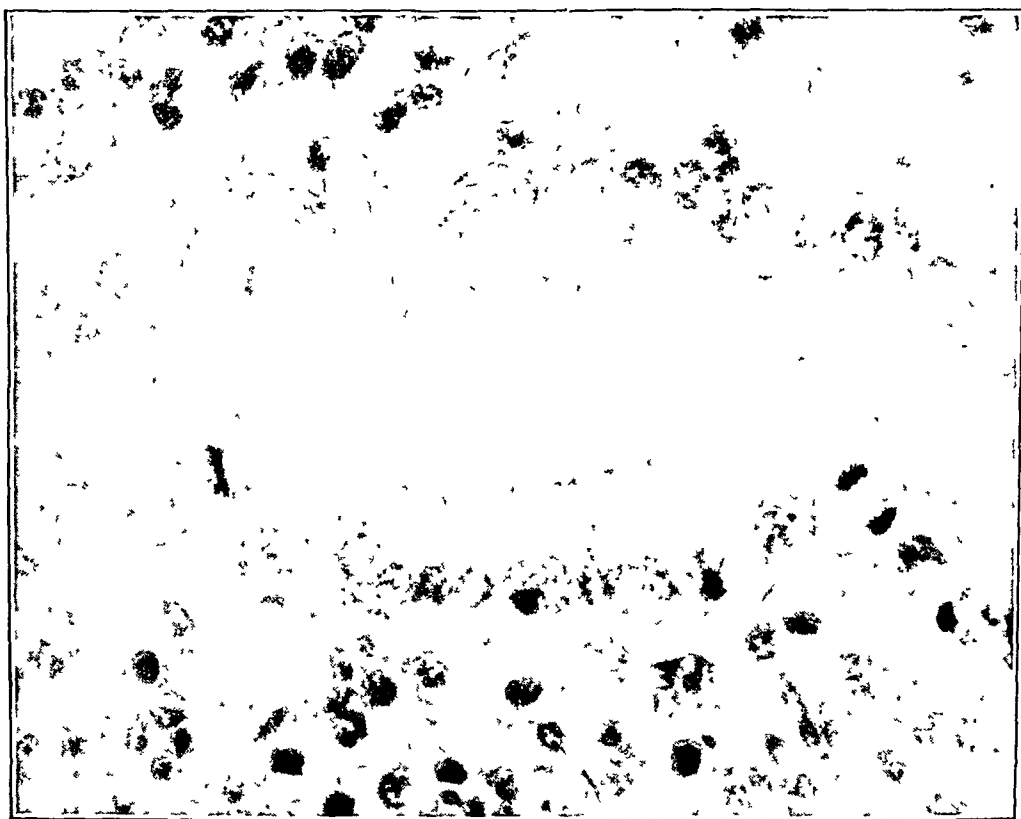


Fig. 4.—High power view of gallbladder mucosa of dog 4, showing frequent mitotic figures.

was thrown into folds. There were frequent mitotic figures in the mucosal cells. Many round cells were seen throughout the wall of the duct.

*Dog 4.*—Dog 4 was killed twenty-four weeks after the sphincter was divided. At necropsy the gallbladder and common duct appeared markedly thickened. The gallbladder could not be aspirated. When it was opened, it was found to contain matted hair. The entrance of the common duct into the duodenum was wide open. Microscopically the gallbladder resembled that of dog 8. The wall was markedly thick-

ened and infiltrated with round cells (fig. 3). Again the frequency of mitotic figures in the mucosal cells was striking (fig. 4). The microscopic sections of the liver showed no evidence of inflammation. The sections of the common duct revealed some increase in connective tissue, with a mild inflammatory reaction in the surrounding connective tissue.

*Dog 6.*—Dog 6 was killed thirty weeks after the sphincter was cut. Grossly the gallbladder appeared normal. The common duct appeared more distinct than usual. Microscopically the gallbladder and liver appeared normal. There was possibly a slight increase in connective tissue about the common duct. The epithelium was thrown up into folds.

*Dog 21.*—This dog was killed eighty-six weeks after the sphincter was cut. During the interim the animal had apparently been in good health. At necropsy a small shrunken gallbladder was found. The common duct was grossly thicker than normal. The opening of the common duct into the duodenum was patulous. Microscopically the liver showed a mild infiltration of polymorphonuclear cells about the small bile ducts. There was a small abscess. The gallbladder was thickened by fibrous tissues laid down mainly in the subserosa.

*Dog 22.*—This dog was killed eighty-nine weeks after the sphincter was cut. The opening of the common duct into the duodenum was patulous. The gallbladder was grossly and microscopically thickened. There were numerous lymphoid follicles beneath the epithelium. The liver appeared normal grossly and microscopically.

#### COMMENT

After transduodenal division of the sphincter of Oddi and division of a portion of the intramural wall of the common duct, a wide opening persists, permitting duodenal contents to regurgitate as high as the gallbladder. The presence of large amounts of diastase in the gallbladder bile after, but not before, the sphincter of Oddi is divided and the finding of hair in the gallbladder of 1 dog substantiate this statement. As described earlier,<sup>6</sup> division of the sphincteric mechanism of the common duct is followed by chronic inflammatory changes in the gallbladder and the common duct. In our experiments these changes were most marked in cases in which the duodenal reflux was the greatest, as shown by higher concentrations of diastase in the gallbladder. In 3 of the 10 dogs hepatitis ensued. This suggests that the division of the sphincter of Oddi in human beings for therapeutic purposes in cases of recurrent pancreatitis should be approached with caution.

6. Colp and others.<sup>2</sup> Mallet-Guy and others.<sup>3</sup> Mallet-Guy and Auger.<sup>4</sup>

High diastase levels have been found in human gallbladder bile on some occasions. In recent years the suggestion has been made that pancreatic juice or duodenal contents may cause disease by entrance into the upper part of the common duct and gallbladder.<sup>1</sup> It is not apparent whether the inflammatory changes observed in these experiments are due to the action of activated pancreatic enzymes or to bacterial action or to both. Mallet-Guy, Auger and Billa<sup>2</sup> found that after transection of the sphincter of Oddi in the dog, the gallbladder bile contains *Bacillus coli* and *Streptococcus viridans*, as well as other habitual residents of the intestine.

The significance of the large number of mitotic figures in the mucosal cells observed in 2 cases is not known. It is of interest that the pathologic changes in the gallbladder induced by regurgitation up the common bile duct consist chiefly of subserosal fibrosis and that Luschka's ducts, which so frequently characterize human chronic cholecystitis, were not found in these gallbladders.

The experimental production of chronic cholecystitis by division of the sphincter of Oddi in dogs suggests that some cases of chronic cholecystitis in human beings might possibly be due to an incompetent sphincter mechanism at the opening of the common duct into the duodenum.

#### SUMMARY

When the sphincter of Oddi in dogs was divided transduodenally, duodenal contents regurgitated into the gallbladder. Chronic cholecystitis and, occasionally, acute hepatitis ensued. Numerous mitotic figures were found in the mucosa of two gallbladders.

# THRESHOLD OF THERMAL TRAUMA AND INFLUENCE OF ADRENAL CORTICAL AND POSTERIOR PITUITARY EXTRACTS ON THE CAPILLARY AND CHEMICAL CHANGES

An Experimental Study

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WITHIN the few years prior to the entry of the United States into World War II there was a growing conviction that adrenal cortical extract was beneficial in the treatment of burn shock. From 1933, when Swingle and others<sup>1</sup> first called attention to the similarity of adrenal insufficiency and shock, there appeared numerous reports of the efficacy of both adrenal cortical extract and desoxycorticosterone acetate in various forms of experimental and clinical shock. Among others, Scudder and Elliott<sup>2</sup> reported benefit from the use of adrenal cortical extract in the care of victims of the Hindenberg dirigible disaster who suffered from shock after burns, and Rhoads, Wolff and Lee<sup>3</sup> expressed the belief that they had observed a plasma-sparing effect of the extract in burned patients. The point of view that adrenal cortical therapy was beneficial in shock seemed plausible, particularly when the shock was due to burns, since the salient physiologic disorder of a thermal injury had been demonstrated to be an increased capillary

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From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. Swingle, W. W.; Pfiffner, J. J.; Vars, H. M.; Bott, P. A., and Parkins, W. M.: The Function of the Adrenal Cortical Hormone and the Cause of Death from Adrenal Insufficiency, *Science* **77**:58, 1933.

2. Scudder, J., and Elliott, R. H. E., Jr.: Controlled Fluid Therapy in Burns, *South. Med. & Surg.* **104**:651, 1942.

3. Rhoads, J. E.; Wolff, W. A., and Lee, W. E.: The Use of Adrenal Cortical Extract in the Treatment of Traumatic Shock of Burns, *Ann. Surg.* **113**:955, 1941.

permeability and because there was experimental evidence suggesting an increased capillary permeability in adrenal insufficiency.<sup>4</sup> Lymph draining from peripheral tissues of dogs suffering from adrenal insufficiency had been demonstrated to have a high protein concentration, one possible explanation of which was an increased capillary permeability.

Neither the clinical nor the experimental observations of the efficacy of adrenal cortical extract in shock were so unequivocal that the concept could be accepted without confirmation. In several of the reports an alternative explanation could be suggested for the positive finding. In the patients the burns and the subsequent wound infections were by no means equal and comparable, and in their care measures other than administration of adrenal cortical extract had been employed. For the experimental findings which lead to the suggestion that the capillaries are more permeable in adrenal cortical insufficiency, an alternative explanation is tenable. The observed increase of the protein concentration in peripheral lymph could be explained on the basis of dehydration. However, even if the hormone of the adrenal cortex exerted no direct influence on the capillary membrane, it might influence renal or metabolic function in such a way as to relieve a load placed on the organism by trauma.

In view of the importance for the care of casualties in World War II of any measure leading to improvement in the therapy of burns, investigation into the use of adrenal cortical hormone substances in the therapy of burn shock was indicated. Two approaches to the study were possible—a physical one through capillary permeability and a chemical one through changes in intermediary metabolism. Because of the interest of this laboratory in the possible role of the adrenal cortex in capillary permeability, it seemed wise to see if the adrenal cortical extract influenced the abnormal permeability induced by thermal trauma in the dog and at the same time to study its influence on the protein, carbohydrate and electrolyte changes of burn shock in the dog and in man.

It is to be recalled that at the time of this study two types of abnormal capillary permeability were believed to exist in burn shock: the first, that at the site of injury and the direct result of heat, had been demonstrated by Drinker and his co-workers,<sup>5</sup> while the second, a

4. Cope, O.; Brenizer, A. G., Jr., and Polderman, H.: Capillary Permeability and the Adrenal Cortex: Studies of Cervical Lymph in the Adrenalectomized Dog, *Am. J. Physiol.* **137**:69, 1942.

5. (a) Field, M. E.; Drinker, C. K., and White, J. C.: Lymph Pressures in Sterile Inflammation, *J. Exper. Med.* **56**:363, 1932. (b) Glenn, W. W. L.; Petersen, D. K., and Drinker, C. K.: The Flow of Lymph from Burned Tissue, with Particular Reference to the Effects of Fibrin Formation upon Lymph Drainage and Composition, *Surgery* **12**:685, 1942.

later peripheral increase in permeability as a result of diminished blood flow, had been postulated.<sup>6</sup> Since it was theoretically possible that the adrenal cortical hormone could affect either type of the abnormal permeability, a more extended survey of the nature of the abnormal permeability of burn shock was made.

In the initial experiments, capillary permeability was judged by observing in dogs the transfer of tagged molecules from blood stream to lymphatic vessel. These experiments have already been reported.<sup>7</sup> Radioactive isotopes in various chemical combinations were used as the tagged molecules. Abnormal capillary permeability was found only in traumatized or infected areas of the body; there was no evidence even in late shock of any generalized increase in permeability. Adrenal cortical extract was given to 3 animals; there was no demonstrable influence on the abnormal permeability in the burned area. The burns of the dogs' feet were severe, however (an immersion in boiling water for fifteen seconds), and because it seemed unreasonable to expect any hormone to exert an influence on necrosed capillaries, the observations were extended by determining the minimal amount of thermal trauma which would give reproducible alteration in capillary permeability and then, on such a preparation, the efficacy of adrenal cortical extract was tested. These experiments are reported in the present paper.

The idea of a controlling influence of extracts of the posterior lobe of the pituitary on the distribution of water within the body has been accepted. Although the posterior pituitary hormone acts on renal excretion of water and on peripheral blood flow, would it not be possible that this hormone might have a direct influence on capillary permeability?

In this paper are reported the effect of increasing temperature and duration of exposure on the capillary permeability of the dog's foot and the failure of adrenal cortical extract and posterior pituitary injection to influence either the abnormal permeability induced by even a minimal burn or the course of the protein, carbohydrate and electrolyte changes which follow a burn in the dog.

#### METHODS

Dogs weighing from 15 to 25 Kg. were used. They were maintained under pentobarbital sodium anesthesia throughout the experiment. A lymphatic trunk of each hindleg was cannulated above the ankle joint as described by Drinker and others.<sup>5a</sup> Burn trauma was produced by immersing the foot and ankle to the level

6. Moon, V. H.: *Shock and Related Capillary Phenomena*, New York, Oxford University Press, 1938.

7. Cope, O., and Moore, F. D.: *A Study of Capillary Permeability in Experimental Burns and Burn Shock Using Radioactive Dyes in Blood and Lymph*, J. Clin. Investigation **23**:241, 1944.



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of the lymphatic cannula in water of known temperature for a specific time. The degree of trauma was judged by the change in lymph flow and in the concentration of the total and other proteins. The flow of lymph in these trunks is sluggish in the unburned resting dog under pentobarbital sodium anesthesia, and in order to obtain an adequate volume of lymph for control analysis it was usually necessary to stimulate the flow by gentle massage of the footpads. This massage was made as much as possible to simulate the pressure of walking in order to avoid mechanical

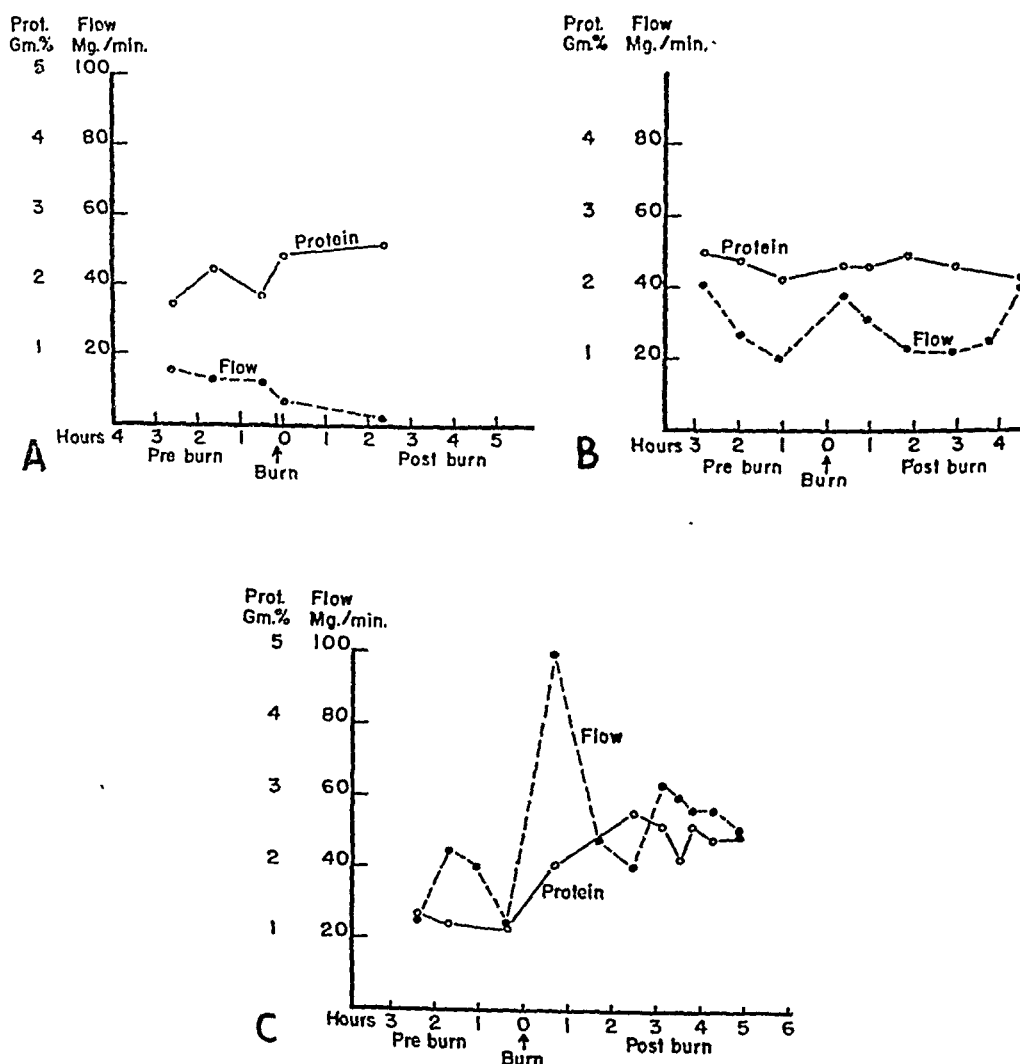


Chart 1.—*A*, lack of effect of subthreshold burn on lymph flow and protein concentration. The dog's foot was immersed in water at 60 C. for 10 seconds. *B*, increase in flow of lymph without change in protein concentration after subthreshold burn. The foot was immersed in water at 65.5 C. for 10 seconds. *C*, effect of threshold burn on lymph flow and protein concentration. Burn by water at 67 C. for 10 seconds. There is a significant rise in both flow and protein concentration.

trauma. After the trauma of a burn, the lymph flow is spontaneous; massage is not necessary and was not used. The amounts of lymph flow before and after burn are therefore not absolutely comparable, the amount recorded before burn being higher than the actual amount. The initial flow recorded before burn is further

increased above the actual amount by the transient obstruction incident to cannulation. The total protein concentration of lymph has been shown by Drinker to represent a measure of capillary permeability, provided the flow of lymph is maintained and the serum protein concentration is unaltered.

The mean arterial blood pressure was recorded periodically with a mercury manometer by puncturing the carotid artery with a needle, without interruption of the blood flow. All blood determinations were made on arterial blood taken from the carotid artery. The blood plasma, serum and lymph total protein levels were measured by the refractometer. In a number of the experiments these determinations were checked by the Kjeldahl method. When an albumin-globulin ratio is determined, when the nonprotein nitrogen is increased or when the plasma or lymph is fatty or hemolyzed, the refractometer protein value is always checked by the chemical method. Hematocrit values were determined on heparinized blood. Other chemical determinations were made by standard chemical methods.

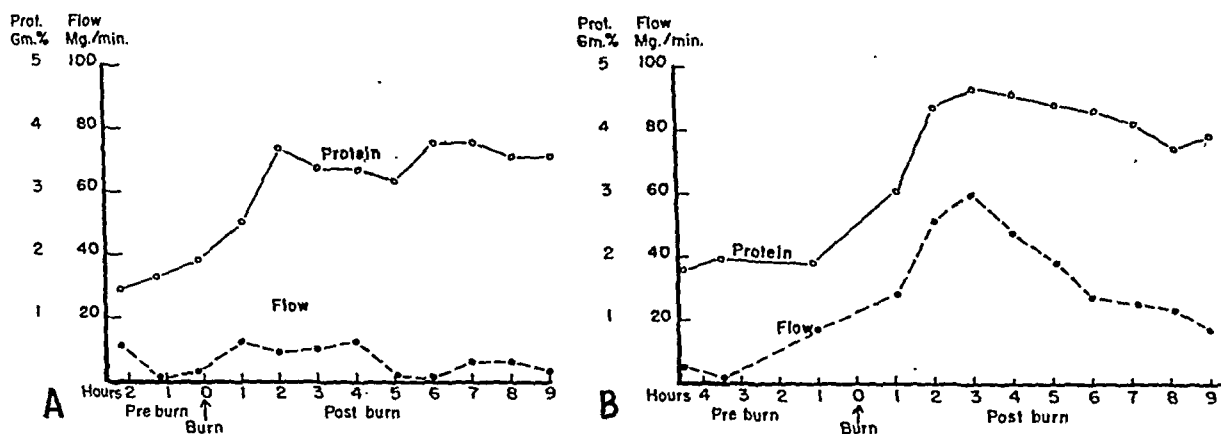


Chart 2.—*A*, the least effect of the minimal burn of water at 70 C. for 10 seconds. The protein concentration of the lymph rose to 3.5 Gm. per hundred cubic centimeters while the flow increased only perceptibly. *B*, the maximal effect of the minimal burn of water at 70 C. for 10 seconds. The protein concentration of the lymph rose to 4.5 Gm. per hundred cubic centimeters; the increase in the flow was moderate.

#### EXPERIMENTS

1. *Threshold of Burn Trauma.*—In this group of experiments the minimal burn of the dog's foot which would yield reproducible changes in lymph flow and total protein concentration was determined.

Little information was available to guide us. Drinker's observations, with one exception, had been made with the use of boiling water with an immersion period of two minutes, which produced a severe necrosing burn. In the exception, the temperature of the bath in which the dog's feet were constantly immersed was slowly raised; the first increase in lymph flow was recorded between 50 and 60 C.

After a control period of two to four hours during which control samples of lymph were collected for analysis, the dogs' feet and ankles

were submerged in water varying from 60 to 100 C. The immersion time chosen was ten seconds. Immersion in the 60 C. bath was followed by no significant alteration in lymph flow or total protein concentration (chart 1*A*). There was actually a drop in flow, but this is accounted for by cessation of massage. The slight rise in

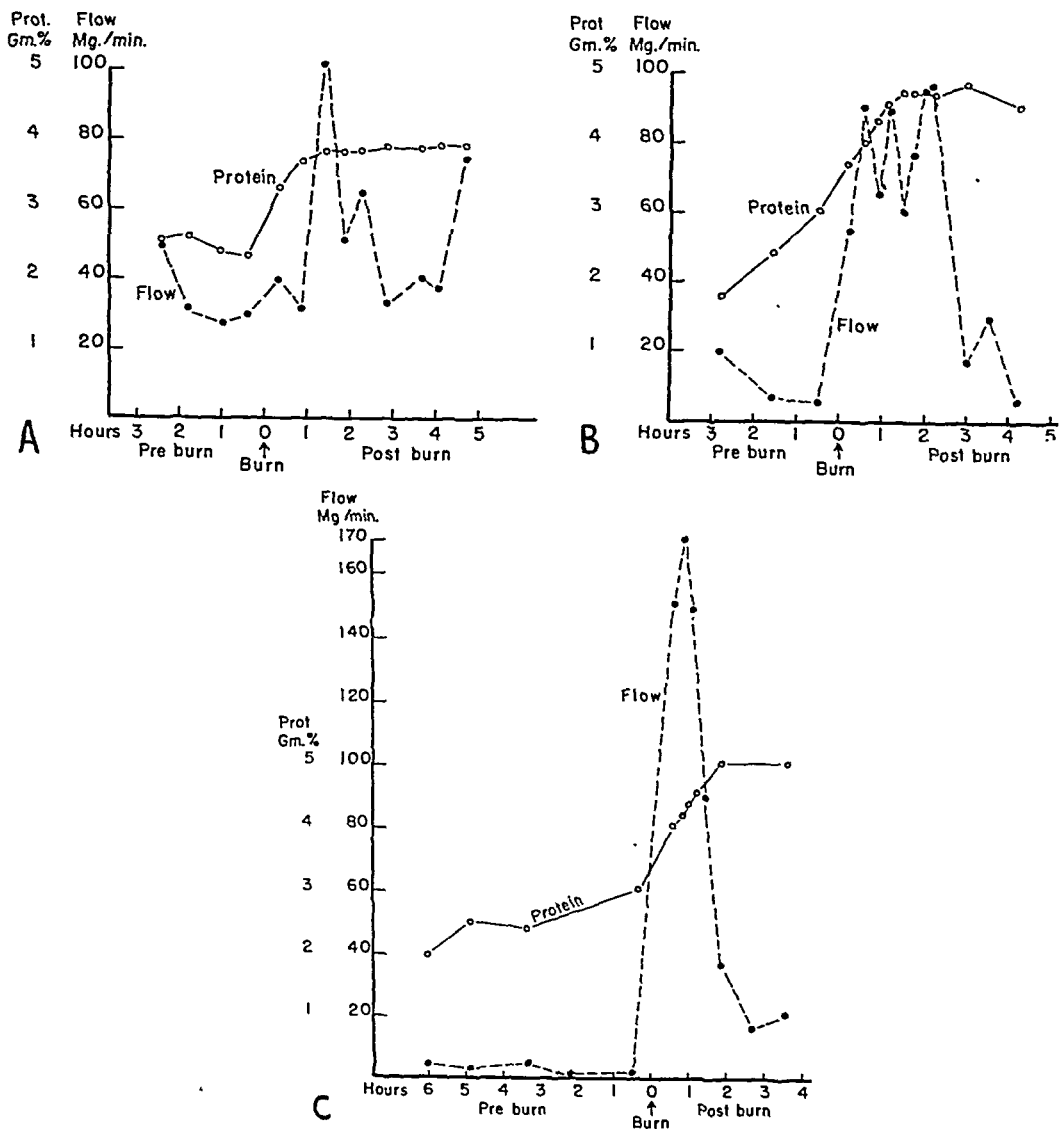


Chart 3.—*A*, the effect of a greater than minimal burn of water at 75 C. for 10 seconds. Although the change in protein concentration is no greater than that following a threshold burn, the rise in flow is. *B*, the effect of a moderate burn of water at 80 C. for 10 seconds. The rise both in protein concentration and in flow is significantly greater than that encountered after a mild or threshold burn. *C*, the effect of a severe burn of water at 100 C. for 20 seconds. The rise in protein concentration to 5 Gm. and of the flow to 170 mg. per minute within the first two hours after burn represent the maximal changes encountered.

protein concentration encountered is no greater than that to be expected after a period of massage.

After immersion at 65.5 C. there was a recognizable increase in the flow of the lymph (chart 1B). There was, however, no change in protein concentration. After immersion at 67 C. not only the lymph flow but also the protein concentration rose sharply from 1.2 to 2.5 Gm. (chart 1C): this is considered to constitute a threshold burn.

After immersion at 70 C. there was always a rise in both the flow and the protein concentration of the lymph, but the degree of rise was not consistent in the nine experiments carried out at this temperature. In chart 2A are shown the minimal rises and in chart 2B the maximal rises encountered. The rises in flow varied at their peaks from 12 to 62 mg. per minute, while the total protein concentration varied from 3.2 to 4.6 Gm. per hundred cubic centimeters. Because the changes were above the minimum observable and consistently present even though not consistent in degree, this temperature and duration of exposure were chosen as the standard for the assay of the hormones as possible therapeutic agents. The resulting injury constitutes a minimal burn.

Immersion at 75 C. and at 80 C. was followed by increasing rises in both lymph flow and protein concentration (chart 3A and B). At 80 C. the total protein concentration reached 4.5 Gm. or above, the concentration found with the severe burns made with boiling water. The flow, however, was still below the maximal. In chart 3C are depicted the consequences of immersion at 100 C. for twenty seconds. There is an abrupt rise in both flow and protein concentration, the flow reaching 170 mg. per minute in an hour and the protein concentration 5.0 Gm. in two hours. These changes are maximal. In experiments with a more prolonged immersion time, neither lymph flow nor total protein concentration registered the increasing necrosis. Other changes, such as rate of edema formation and hemolysis in both lymph and serum, did reflect the increasing degree of tissue damage. The more prolonged the immersion in boiling water, the more rapid the tissue swelling.

Hemolysis was not observed following burns of 80 C. or less. The red pigment of hemolysis was grossly and consistently visible in the lymph after exposure to 100 C. for twenty seconds. With increasingly severe burns the intensity of hemolysis was augmented so that a burn at 100 C. for two minutes was immediately followed by a deep pink in the lymph draining from the burned area, and if two or more feet were burned there was delayed, grossly visible pigmentation of the blood plasma.

2. *Effect of Adrenal Cortical Extract on Permeability.*—The effect of adrenal cortical extract<sup>8</sup> on the abnormal capillary permeability

8. The Upjohn Company provided us with a generous supply of the aqueous extract of the cortex of the adrenal gland.

induced by a minimal burn was assayed in 8 dogs. The extract was administered within the first hour after the burn. Both hind feet and ankles of each dog were burned and the lymph changes of each wound recorded. The immersion temperatures were approximately 70 C. except for 3 feet immersed at 64.5, 68 and 73 C. The immersion time was ten seconds. No significant differences in lymph flow or protein concentration from those of the controls in this temperature range were observed. The findings in typical experiments are shown in chart 4.

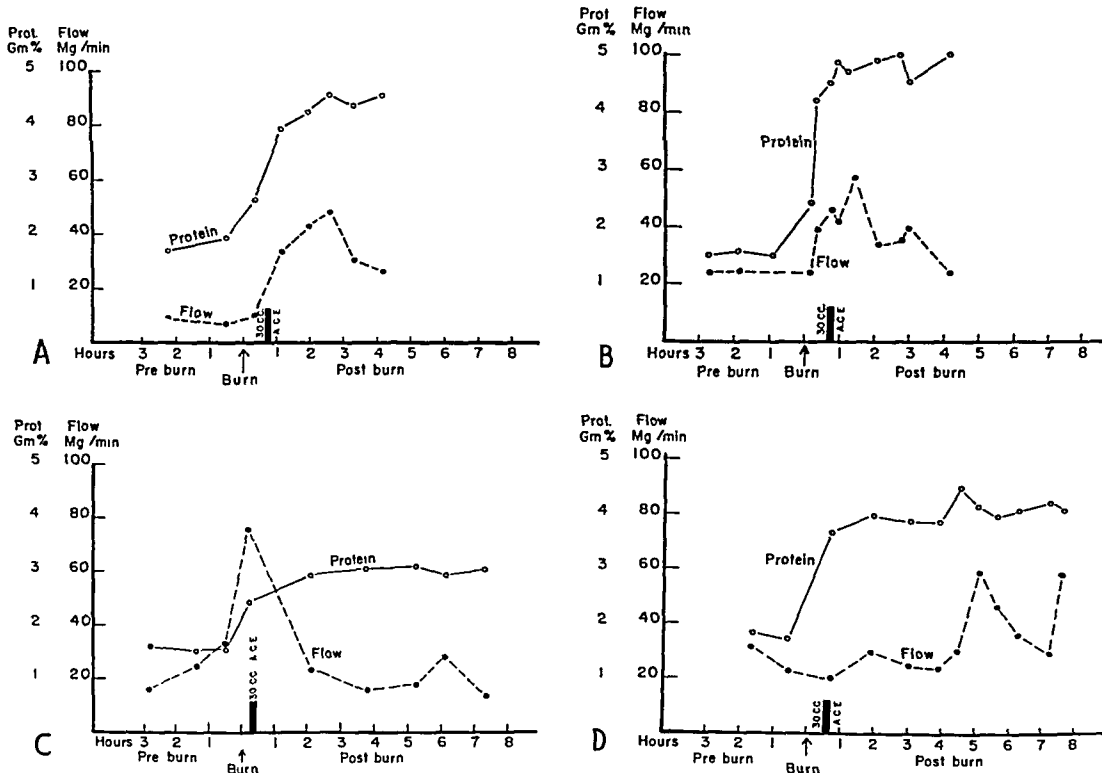


Chart 4.—*A*, lack of effect of adrenal cortical extract on lymph protein and flow after a threshold burn at 68 C. for 10 seconds. The changes observed are comparable to those encountered after a burn of similar severity in an untreated dog. *B*, lack of effect of adrenal cortical extract on the lymph flowing after a greater than minimal burn, 73 C. for 10 seconds. *C*, lack of effect of adrenal cortical extract on the lymph flow after a subthreshold burn, 64.5 C. for 10 seconds. *D*, lack of effect of adrenal cortical extract on the lymph flow after a minimal burn, 70.5 C. for 10 seconds.

3. *Effect of Posterior Pituitary Injection on Permeability.*—Extract of the posterior lobe of the pituitary gland (pitressin® [Parke, Davis & Co.]) was injected intravenously into 3 dogs whose hind feet and ankles had been burned by water at 70 C. for ten seconds. The first injection was given approximately one hour after the burn.

A second injection was given four to five hours later; the dog of the first experiment died immediately after this second injection.

The protein concentration of the lymph fell transitorily after the administration of the pituitary extract in four of the five observations. The fall was but 0.2 to 0.5 Gm. per hundred cubic centimeters and was apparent at one-half hour after the injection; at one and one-half hours after injection the concentration had returned to the preinjection level (chart 5). No such consistent change took place in lymph flow. From one-half of the wounds there was a decrease in flow starting

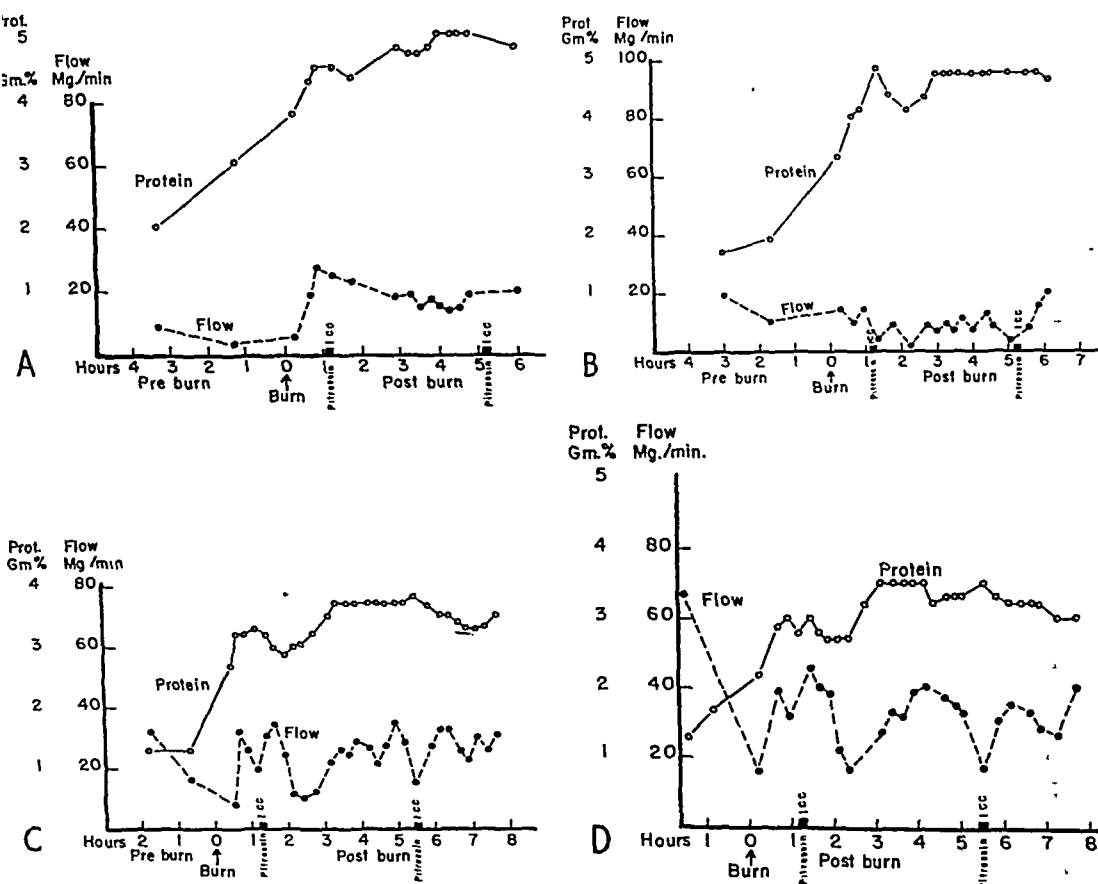


Chart 5.—*A*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. There was a slight fall in the protein concentration immediately after the injection. *B*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. The fall in protein concentration immediately after the injection was greater than that encountered in the experiment recorded in chart 5 *A*. *C*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. After each injection there was a transient fall in protein concentration. *D*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. The protein concentration is more irregular and the fall following each injection is less obvious than in the experiment recorded in chart 5 *C*.

one hour after injection, but after other injections there was a rise during the same period. The flow from the two feet of the same animal did not always change in parallel fashion.



Blood pressure changes were recorded throughout the experiments. In the first experiment the blood pressure was not followed during the injection, but it had fallen from 160 mm. of mercury before

TABLE 1.—A. Chemical Observations on Blood

Dog	Time	Hours	Arterial Blood																	
			Blood Pressure, Mm. Hg.	Hematocrit Value, per Cent Cells	Total Protein, Gm. per 100 Cc.	A/G Ratio	Fibrinogen, Gm. per 100 Cc.	Amylase	Cholinesterase	Nonprotein Nitrogen, Mg. per 100 Cc.	CO <sub>2</sub> , mEq. per Liter	Cl, mEq. per Liter	P, Mg. per 100 Cc.	Total Base, mEq. per Liter	Na, mEq. per Liter	K, mEq. per Liter	Ca, Mg. per 100 Cc.	Plasma Blood		
																		Lactic Acid, Mg. per 100 Cc.	Pyruvic Acid, Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.
A. Observations on																				
B 1	Before burn.....	..	...	47	7.1	...	...	11.2	10.5	25	25.0	114	3.2	155	144	3.9	5.7	...	...	100
	After burn.....	6	107	62	7.7	...	...	10.3	12.0	21	22.0	118	5.3	155	140	4.4	5.5	...	...	...
B 2	Before burn.....	..	143	40	6.7	...	...	13.7	...	74	24.0	117	...	152	140	3.8	5.6	...	...	99
	After burn.....	4	139	53	6.7	...	...	12.9	7.6	74	21.0	116	5.5	158	147	4.1	5.6	21.0	3.6	83
B11	Before burn.....	..	...	43	6.5	...	0.23	...	...	..	...	...	...	...	...	...	...	...	...	...
	After burn.....	3	148	51	7.1	...	0.34	...	...	..	...	...	...	...	...	...	...	...	...	...
B12	Before burn.....	..	136	45	6.3	...	0.27	...	...	..	...	...	...	...	...	...	...	...	...	...
	After burn.....	4	156	49	6.8	...	0.32	...	...	..	...	...	...	...	...	...	...	...	...	...
B13	Before burn.....	..	160	40	6.2	...	0.38	...	...	..	...	...	...	...	...	...	...	...	...	...
	After burn.....	4	186	52	6.9	...	0.39	...	...	..	...	...	...	...	...	...	...	...	...	...
B21	Before burn.....	..	180	47	6.3	1.5	...	13.3	10.5	96	19.2	108	6.6	...	136	2.8	5.0	11.3	2.9	192
	After burn.....	6	160	..	6.1	...	...	15.0	...	110	12.2	110	8.2	144	...	...	...	30.8	3.2	230
	After burn.....	21	60	74	7.5	0.6	...	17.4	12.9	177	12.6	106	13.7	160	137	...	4.7	80.4	5.3	210
B. Observations on Dogs Treated																				
B 9	Before burn.....	..	115	44	6.6	2.5	...	13.5	...	28	27.0	114	5.4	153	146	3.6	5.5	7.7	0.8	143
	After burn: Adrenal cortical extract.....	0.5+16	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	After burn.....	28	161	65	5.8	3.5	...	9.5	...	104	13.9	110	8.4	158	146	5.6	5.1	40.0	3.6	161
B14	Before burn.....	..	195	43	6.4	...	0.51	...	...	..	...	...	...	...	...	...	...	...	...	...
	After burn: Adrenal cortical extract.....	0.5	...	...	...	...	...	...	...	..	...	...	...	...	...	...	...	...	...	...
	After burn.....	3.5	203	62	7.4	...	0.63	...	...	..	...	...	...	...	...	...	...	...	...	...
B20	Before burn.....	..	110	40	7.6	1.2	...	13.9	7.9	37	22.0	114	5.9	152	142	...	4.7	13.6	1.7	242
	After burn: Adrenal cortical extract.....	0.7	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	After burn.....	6	95	47	7.8	1.1	...	11.7	...	31	23.3	110	7.2	152	...	...	...	8.4	2.2	154
	After burn.....	21	82	52	7.7	1.0	...	9.5	...	37	14.6	115	8.7	151	141	2.2	5.0	15.6	2.7	174
	After burn.....	24	68	49	7.3	1.1	...	9.6	...	57	12.1	115	9.9	147	138	2.4	5.1	21.7	2.6	170
	After burn.....	30	55	48	7.1	1.0	...	9.1	7.9	73	11.9	115	10.5	158	141	2.6	5.1	20.5	2.3	179
B24	Before burn.....	..	155	45	6.7	0.7	...	10.9	...	15	23.5	113	3.3	156	141	2.7	4.3	4.0	5.0	133
	After burn.....	5.5	56	60	7.0	0.6	...	9.1	...	15	18.3	121	4.3	164	140	...	4.2	8.7	1.4	171
	After burn: Adrenal cortical extract.....	18.5	...	...	...	...	...	...	...	60	15.0	114	8.6	...	...	...	...	55.0	6.0	256
	After burn: Adrenal cortical extract.....	20	37	62	6.2	0.6	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	After burn.....	20.5	...	63	6.3	0.6	...	8.2	...	73	13.7	99	11.1	162	139	10.6	4.3	65.0	4.0	256

injection to 150 mm. thirteen minutes after injection. At thirty-one minutes the blood pressure had returned to 156 mm. Immediately after the second injection, which was given rapidly, there was a pre-

Lymph																							
Leg												Cervical						Thoracic					
Total Protein, Gm. per 100 Cc.	A/G Ratio	Fibrinogen, Gm. per 100 Cc.	Amylase	Cholinesterase	Nonprotein Nitrogen, Mg. per 100 Cc.	Ca, Mg. per 100 Cc.	Cl, mEq. per Liter	Sugar, Mg. per 100 Cc.	Total Protein, Gm. per 100 Cc.	A/G Ratio	Amylase	Nonprotein Nitrogen, Mg. per 100 Cc.	Ca, Mg. per 100 Cc.	Cl, mEq. per Liter	Sugar, Mg. per 100 Cc.	Total Protein, Gm. per 100 Cc.	A/G Ratio	Amylase	Cholinesterase	Nonprotein Nitrogen, Mg. per 100 Cc.	Ca, Mg. per 100 Cc.	Cl, mEq. per Liter	Sugar, Mg. per 100 Cc.
Untreated Dogs																							
2.0 4.3	...	....	9.8	3.9	32	5.0	124	141 134	2.8 3.2	...	8.7 8.4	36	5.2	120	143	4.3 4.6	...	9.8 9.8	...	21 32	5.1 5.5	119 118	144 123
2.3 4.4	...	....	12.7	...	122	5.2	117	125 136	3.3 2.8	...	12.0 12.4	126 133	...	119 119	119 141	3.5 4.1	...	10.9 10.4	...	84 81	4.8 4.7	118 118	...
2.4 4.8	...	....	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
2.5 3.8	...	0.06 0.11	....	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
1.2 2.5	...	0.13	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	...	...	...	...
2.3 4.3 4.7	...	....	....	...	...	...	...	153 ... 230	3.2 3.2 3.8	...	13.3 ... 12.3	100 ... 141	...	119 ... 117	180 ... 228	5.4 ... 4.3	...	15.1 ... 16.2	...	117 ... 120	4.1 ... 3.9	119 ... 117	192 ... 220
with Adrenal Cortical Extract																							
2.0	...	....	....	...	34	...	120	145	3.5	...	....	35	...	122	145	4.7	3.3	13.1	...	33	5.0	118	151
4.9	1.7	....	14.3	...	28	5.3	117	151	3.2	4.0	12.5	67	4.2	120	153	4.5	3.5	13.7	...	90	4.7	118	149
1.8	...	....	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	...	...	...	...
4.5	...	....	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	...	...	...	...
2.8	...	....	....	...	...	...	...	238	4.2	...	....	...	...	...	230	...	...	....	...	...	...	...	...
6.2 7.3 5.5 ...	...	....	....	...	...	...	...	...	5.2 5.8 5.4 5.5	...	...	...	...	...	...	...	...	....	...	...	...	...	...
1.0 1.2	...	....	....	...	22	...	...	137 ...	3.8 4.1	1.4 1.3	11.5 ...	16 16	...	121 122	146 170	4.7 4.8	0.5 0.6	9.5 9.6	...	15 24	3.8 3.9	119 123	132 147
1.2	...	....	....	...	...	...	...	154	3.6	0.6	7.3	33	...	118	246	4.9	0.4	7.4	...	43	4.0	121	...
2.5	...	....	9.1	...	...	...	...	242	3.8	...	....	...	...	...	...	5.3	0.8	16.3	...	59	4.2	117	250

pressure was followed throughout each injection. In 1 dog (chart 5*A* and *B*) the blood pressure rose 5 and 17 mm. during the injections but fell to 100 and 13 mm. below the preinjection levels at fifteen

and twenty minutes after injection. There was a gradual return toward the preinjection level during the subsequent hour. In the other experiments (chart 5C and D), the blood pressure did not rise during the injections, but at fifteen minutes after the injections the pressure was 9 and 11 mm. higher than before, and it returned to the preinjection levels during the second fifteen minutes.

Respirations ceased during the first injection in the second experiment, but the animal survived after a short period of artificial respiration. In the final experiment the respirations were slowed by the first injection.

4. *Chemical Changes of Burn Shock and the Influence Thereon of Adrenal Cortical and Posterior Pituitary Extracts.*—A burn has long been known to be followed by changes in concentration within the extracellular fluid of the electrolytes, chlorides, sodium and potassium and of proteins in the plasma and to cause a rise in blood sugar.<sup>9</sup> The hormone of the adrenal cortex has been shown to influence the concentration and balance of these same electrolytes and carbohydrate metabolism.<sup>10</sup> The hormone of the posterior lobe of the pituitary gland not only causes retention of water but also affects carbohydrate metabolism.<sup>11</sup> An object was, therefore, to see to what extent the extracts of these two glands might influence the changes which follow a burn.

The changes in protein concentration of the plasma, the result of the loss of protein into the wound area, are reported elsewhere.<sup>12</sup> Comparable alterations in protein concentration of the serum were found in the dogs burned and treated with adrenal cortical extract (table 1). In three of the experiments with the adrenal cortical extract the amylase activity of the serum and cervical and thoracic lymph was observed (table 1B B9, B20 and B24). Slight decreases were found in the activity in the serum and either an increase or no change in that of the lymph. In all cases the total protein concentration changed in the same direction. The changes in amylase activity and protein concentration were within the limits observed in the control animals, which were burned but not given extract.

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9. Harkins, H. N.: *The Treatment of Burns*, Springfield, Ill., Charles C Thomas, 1942.

10. Swingle, W. W., and Remington, J. W.: *The Role of the Adrenal Cortex in Physiological Processes*, *Physiol. Rev.* **24**:89, 1944.

11. Burn, J. H.: *The Modification of the Action of Insulin by Pituitary Extract and Other Substances*, *J. Physiol.* **57**:318, 1923.

12. Cope, O.; Graham, J. B.; Moore, F. D., and Ball, M. R.: *The Nature of the Shift of Plasma Protein to the Extravascular Space Following Thermal Trauma*, *Ann. Surg.* **128**:1041, 1948.

Cholinesterase activity was observed in the serum of 1 control and of 1 dog treated with cortical extract. There was a slight rise in activity in the control paralleling the rise in serum protein (B21). In the treated dog the activity did not change but the total protein fell from 7.6 to 7.1 Gm. (B20).

Changes in the albumin-globulin ratio after burning and differences in the ratio between blood and lymph were not consistent. The ratio in thoracic duct lymph tended to be higher than that in serum, as previously reported.<sup>13</sup> The fibrinogen content ran closely parallel to the total protein concentrations in both serum and lymph; there was thus no evidence of loss of fibrinogen in the wound area.

The effect of the pentobarbital sodium anesthesia was controlled in 3 animals (table 2). The changes in hematocrit value, serum pro-

TABLE 2.—*The Effect of Pentobarbital Sodium Anesthesia on the Hematocrit Value, Serum Total Protein and Nonprotein Nitrogen in Dogs*

Dog	Time	Hours	Arterial Blood		
			Hemato- crit Value, % Cells	Serum	
				Protein, Gm./100 Cc.	NPN
NC1	After pentobarbital sodium.....	1.33	40	6.2	32
	After pentobarbital sodium.....	22	55	6.1	24
	After pentobarbital sodium.....	31.5	69	7.0	47
NC2	After pentobarbital sodium.....	1	41	6.7	61
	After pentobarbital sodium.....	10	57	6.7	34
	After pentobarbital sodium.....	20	49	6.6	42
	After pentobarbital sodium.....	26	43	5.9	37
ION1	Before pentobarbital sodium.....	..	45	7.0	63
	After pentobarbital sodium.....	4.5	45	7.0	52
	After pentobarbital sodium.....	10	50	7.0	48
	After pentobarbital sodium.....	31.5	49	7.2	39
	After pentobarbital sodium.....	52	57	7.2	40

tein and nonprotein nitrogen were not consistent, but they may be interpreted as indicating slow, moderate dehydration.

The results of the total protein concentration, albumin-globulin ratio and enzyme activities are interpreted to mean that under the conditions of these experiments the adrenal cortical extract had no effect on the permeability of the capillary to these proteins.

The potassium and phosphorus concentrations rose in the extracellular fluid after the burn. There was no change in the serum and lymph sodium and serum chlorides. (The determinations in lymph of sodium, potassium, total base and phosphorus are not recorded in the tables because they were not significantly different from those of the serum.) The chloride and calcium content of the lymph from the leg after the burn fell and rose respectively in amounts to be expected

13. Drinker, C. K., and Yoffey, J. M.: *Lymphatics, Lymph and Lymphoid Tissue*, Cambridge, Mass., Harvard University Press, 1941.

from the rise in protein concentration. These changes are consistent with either a generalized cellular dehydration or release of these ions from the wounded cells. No significant difference was observed between the control animals and those treated with cortical extract.

The burn was followed by a sharp rise in lactic and pyruvic acid levels of the blood plasma (table 1). Comparable levels were found in the various lymphs whenever measured and are therefore not recorded. The blood and lymph sugar levels, increased after administration of pentobarbital sodium, remained increased or rose further after the

TABLE 3.—*The Chemical Observations in Blood Serum, Plasma and Lymph in Burned Dogs Treated with Posterior Pituitary Extract*

Dog	Time	Hours	Arterial Blood														Leg Lymph	
			Blood Pressure, Mm. Hg.	Hematocrit Value, per Cent	Protein, Gm./100 Cc.	pH	Serum						Plasma		Blood Sugar, Mg./100 Cc.	Total Protein, Gm./100 Cc.	pH	CO <sub>2</sub> , mEq./Liter
							CO <sub>2</sub> , mEq./Liter	Cl, mEq./Liter	P, Mg./100 Cc.	Total Base, mEq./Liter	Na, mEq./Liter	K, mEq./Liter	Lactic Acid	Pyruvic Acid				
B 25	Before burn	..	164	37.7	5.9	7.38	28.0	116	3.9	157	149	3.6	5.2	0.9	152	...	7.59	30.0
	After burn	0.8	150	38.7	...	....	....	...	...	152	...	...	...	...	152	...	7.60	27.4
	Posterior pituitary extract	1																
	After burn	2	150	40.5	6.1	7.35	25.6	114	4.4	158	143	4.7	17.0	2.3	139	...	....	....
	After burn	3	160	40.3	6.1	7.39	26.9	114	4.1	157	143	4.0	6.8	5.0	159	...	7.59	27.5
B 26	Before burn	..	150	43.6	7.9	7.55	....	...	...	...	...	...	...	...	...	1.9	7.66	....
	After burn	1	145	46.5	7.9	7.57	....	...	...	...	...	...	...	...	...	...	7.61	....
	Posterior pituitary extract	1																
	After burn	3	140	51.0	8.1	7.25	....	...	...	...	...	...	...	...	...	4.5	7.61	....
B 27	Before burn	..	120	39.4	6.5	7.39	....	...	5.7	...	...	...	5.5	0.8	135	1.7	7.37	....
	After burn	1	124	42.3	6.8	7.35	....	...	4.7	...	...	...	6.0	0.9	147	2.8	7.37	....
	Posterior pituitary extract	1																
	After burn	2	116	47.5	6.8	7.25	....	...	4.7	...	...	...	11.6	0.2	148	3.2	7.37	....
	After burn	4	117	47.2	7.0	7.27	....	...	5.6	...	...	...	5.6	0.8	139	3.2	7.38	....
	Posterior pituitary extract	6																
	After burn	10	118	50.0	7.2	7.30	....	...	4.6	...	...	...	5.5	1.3	150	3.0	7.37	....

burning. There were no differences between the control animals and those treated with cortical extract. In 3 animals the effect of pituitary extract was observed (table 3). With the dosage employed, there was no significant difference from the controls (table 1 A).

#### COMMENT

The thesis on which these experiments were undertaken, that the extract of the adrenal cortex is beneficial in burn shock, is not substantiated. Neither a sparing action on the loss of plasma into a burn wound nor a reversal of the pattern of electrolyte and metabolic change was found. Loss of plasma stems from increased permeability of the capil-

laries of the wound, and no effect on this increased permeability was observed. The beneficial action of substitution therapy in the adrenalectomized, cortically insufficient animal was not duplicated in the burned animal even though the abnormal electrolyte pattern of the extracellular fluid of the 2 animals is similar.

The negative findings in these experiments with adrenal cortical extract are not to be construed to mean that the cortical hormone is without influence on capillary permeability or that it does not sway the course of shock following burns by some as yet hidden metabolic effect. It is clear from Selye's description of the adaptation reaction that the adrenal cortex is stimulated to overactivity by trauma.<sup>14</sup> Hypersecretion of the adrenal cortex in the human being as part of the reaction to a burn has been amply proved.<sup>15</sup> Just what this response of the adrenal cortex means to the organism, however, is still obscure, and it is undetermined whether heightened cortical function from the administration of extract is desirable. It is certain that adrenal cortical extract should not be given to an extensively burned patient with the idea that it will diminish the amount of plasma or water loss or the need for protein, electrolyte and fluid therapy.

The experiments with posterior pituitary extract also point to no beneficial effect to be obtained in burn shock from the use of this hormone. Under the conditions of the experiments, no action on the abnormal capillary permeability of the burn wound was demonstrated. The transitory drop in protein concentration of the lymph flowing from the wound after administration of posterior pituitary extract should not lead to the use of this hormone in an effort to decrease loss of plasma; the drop is more likely to be due to a decrease in arteriolar blood flow and capillary pressure than to a change in capillary permeability. The arteriolar constriction presumably is not limited to the burn wound, and indeed fatal constriction of the coronary artery has been described. To advise against the use of posterior pituitary hormone in burn shock, however, is not stating that the posterior lobe of the pituitary is not called on for extraordinary secretion during the dehydration phase of burn shock.

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14. Selye, H.: The General Adaptation Syndrome and the Diseases of Adaptation, *J. Clin. Endocrinology* **6**:117, 1946.

15. Browne, J. S. L.: Personal communication to the author, 1942. Cope, O.; Nathanson, I. T.; Rourke, G. M., and Wilson, H.: Symposium on the Management of the Cocoanut Grove Burns at the Massachusetts General Hospital: Metabolic Observations, *Ann. Surg.* **117**:937, 1943. Shipley, R. A.; Dorfman, R. I.; Buchwald, E., and Ross, E.: The Effect of Infection and Trauma on the Excretion of Urinary Cortin, *J. Clin. Investigation* **25**:673, 1946. Talbot, N. B.; Nathanson, I. T., and Cope, O.: Unpublished Data.

## SUMMARY

The efficacy of extracts of the adrenal cortex and posterior lobe of the pituitary gland in the treatment of burn shock has been tested in the anesthetized dog; the test objects used were the increased capillary permeability in the burned foot and the changes in intermediary metabolism of protein, carbohydrate and electrolytes induced by the burn.

The threshold of burn trauma which registers as an increase in flow and protein concentration of the lymph draining from the burned foot of the dog was found to be an immersion for ten seconds in hot water of 67 C. Minimal and consistent increases were produced by immersion for ten seconds in water of 70 C. Burns of greater severity are followed by more precipitous and higher rises in lymph flow and protein concentration, more rapid edema formation and hemolysis.

The possible influence of the glandular extracts on the increased capillary permeability was tested on threshold and minimal burns. No effect of the adrenal cortical extract was demonstrable. The use of posterior pituitary extract was followed by a slight, transitory drop in protein concentration of the lymph.

The changes in intermediary metabolism observed following burns were also not influenced by the gland extracts.

No evidence was obtained to substantiate the concepts that these gland extracts are useful in the treatment of burn shock.

# EFFECT OF THERAPEUTIC COLD ON THE CIRCULATION OF BLOOD AND LYMPH IN THERMAL BURNS

An Experimental Study

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A CHILD soon learns that cold relieves the pain of a burn, and cold has been used since ancient times in the treatment of burns. More recently, at the beginning of the second World War, Webster and others<sup>1</sup> and White and his associates<sup>2</sup> recommended cold in the therapy of immersion foot. They found not only that it relieved the pain but also that it was followed by some reduction in volume of the edema. Should such reduction in edema be achieved in a burn the use of cold might materially reduce the volume of plasma needed in the therapy of burn shock.

There are also theoretic reasons pointing to the use of cold for burns. Cold should diminish the metabolic demands of the wound, and if the circulation to the wound were impaired, the degree of tissue damage might be decreased. Bacterial infection should be reduced by the established effect of cold in decreasing bacterial growth.

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From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. Webster, D. R.; Woolhouse, F. M., and Johnston, J. L.: Immersion Foot, *J. Bone & Joint Surg.* **24**:785, 1942.

2. White, J. C.: Vascular and Neurologic Lesions in Survivors of Shipwreck: Immersion-Foot Syndrome Following Exposure to Cold, *New England J. Med.* **228**:211, 1943. White, J. C., and Scoville, W. B.: Trench Foot and Immersion Foot, *New England J. Med.* **232**:415, 1945.



In addition, Drinker and others<sup>3</sup> have stressed the fact that edema may retard the healing of burn wounds; Blalock<sup>4</sup> has reported an increase in survival time of the dog traumatized with a crushing clamp and treated with cold, and F. M. Allen<sup>5</sup> has recommended enthusiastically the use of cold for all forms of trauma. For all these reasons, theoretic and reported, a probe into the rationale for the use of cold in cases of burns was started. The initial experiments observing lymph flow and edema formation were sufficiently suggestive for the experimental program to be extended to include measurement of the arterial circulation.

#### METHODS

Male dogs in good health weighing from 18 to 22 Kg. were chosen for the experiments. In all, 19 dogs were used. Pentobarbital sodium was administered intravenously or intraperitoneally for anesthesia. The skin of both hindlegs and that overlying a carotid artery was prepared by clipping the hair and applying diluted tincture of iodine and alcohol. The operations were performed under aseptic precautions to avoid as much clostridial infection as possible.

The lymphatic trunks running on either side of the vein of both hindlegs were exposed above the ankle; one was cannulated, and the flow of lymph in the other was diverted to the cannula by closing it with a ligature. The flow of lymph was generally so sluggish before the foot was injured that gentle massage to the foot pads was necessary in order to secure sufficient lymph for control analysis. After injury spontaneous flow only was collected. The flow was measured by weight and recorded in milligrams per minute. Powdered heparin was inserted into the open end of the cannula periodically by means of a fine wire to prevent coagulation of lymph protein.

The arterial blood flow into the foot was measured by means of a U tube flow meter inserted into the anterior tibial artery of each hindleg above the ankle (fig. 1). The anterior tibial rather than the femoral artery was used in order to limit the measurement of blood flow as much as possible to that flowing to the tissues to be damaged. The posterior tibial artery was not ligated.

In order to avoid undue loss of blood during the operations heparinization was delayed until the anterior tibial arteries had been isolated and a blood pressure cannula inserted in the carotid artery. Infusion of heparin<sup>6</sup> by continuous drip into a vein in the front of the leg was carried out.

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3. Glenn, W. W. L.; Petersen, D. K., and Drinker, C. K.: The Flow of Lymph from Burned Tissue, with Particular Reference to the Effects of Fibrin Formation Upon Lymph Damage and Composition, *Surgery* **12**:685, 1942. Glenn, W. W. L.; Gilbert, H. H., and Drinker, C. K.: The Treatment of Burns by the Closed Plaster Method, with Certain Physiological Considerations Implicit in the Success of This Technique, *J. Clin. Investigation* **22**:609, 1943.

4. Blalock, A.: A Comparison of the Effects of the Local Application of Heat and of Cold in the Prevention and Treatment of Experimental Traumatic Shock, *Surgery* **11**:356, 1942.

5. Allen, F. M.: Reduced Temperatures in Surgery: III. Experiments on Pelvic and Abdominal Refrigeration with Especial Reference to Traumatic and Military Surgery, *Am. J. Surg.* **55**:451, 1942.

6. The heparin (liquaemin®) was supplied through the generosity of Roche Organon, Inc., of Nutley, N. J.

The anterior tibial arteries were then opened, a glass cannula inserted in each proximal and distal opening and the flowmeters connected to them. The flowmeters (fig. 1) were of the same type as those used in the experiments testing the effect of a restrictive plaster dressing on a burn wound.<sup>7</sup> Blood flow was observed until stable. All readings were made at systole during expiration; each recording was an average of three readings.

The flowmeters were calibrated at the end of each experiment with blood removed from the dog at that time. Although the actual flow through the meter

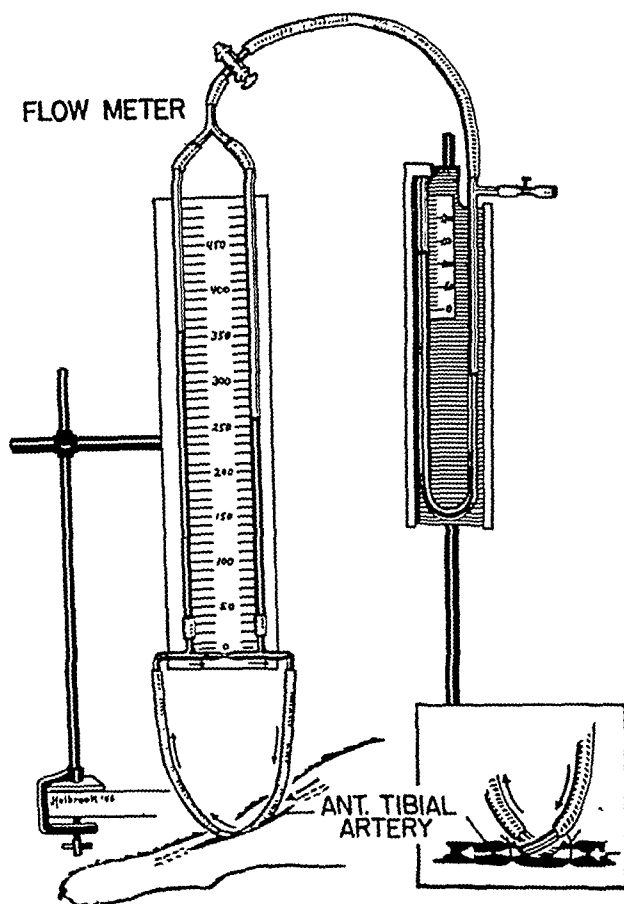


Fig. 1.—Arrangement of U tube flow meter attached to mercury manometer to measure blood pressure. Inset shows glass cannulas inserted into anterior tibial artery of hindleg of dog and connected to flowmeter by means of short segments of rubber tubing. Arrows show direction of blood flow.

during the experiment was thus determined, the amount was presumably not the same as it would have been had the arteries been intact. The presence of the cannulas and the meter inevitably resulted in some obstruction to flow. This factor of obstruction must be kept in mind when interpreting the observations. In spite of

7. See article in this issue entitled "Explorations Into the Physiologic Basis for the Therapeutic Use of Restrictive Bandages in Thermal Trauma: An Experimental Study," page 1056.

the limitation of partial obstruction, the sensitivity of the apparatus to change in blood flow is beyond question.

The sensitivity of the apparatus to change in blood flow was established by control experiments. In several of the experiments, before the feet were subjected to damaging heat the blood flow was measured with the foot immersed in water of 10 C.; a reduction in flow was recorded. Immersion at 40 C. resulted in prompt increase in flow. At the end of one experiment, spinal anesthesia was induced with procaine hydrochloride; a prompt increase in flow took place.

The mean arterial pressure of the blood flow to the wound was measured in the anterior tibial artery by connecting the tops of the U tube with a mercury manometer (fig. 1); it was also recorded in the systemic circulation through the cannula in the carotid artery.

The infusion of heparin was continued intermittently by slow drip throughout the experiment. Because of the heparinization, sufficient blood oozed from the tibial arterial wounds in the majority of the experiments to warrant returning it to the circulation. The oozing blood was collected in a pan, periodically filtered, diluted with isotonic sodium chloride solution and slowly injected intravenously.

The trauma was inflicted by dipping both hindfeet to an identical level just below the ankle in a deep pan of hot water. Temperatures of the water varied from 80 to 100 C.; the duration of immersion was ten or fifteen seconds. Cold used in treatment was applied by a similar water bath technic, the temperature of the water being 10 C. The bath of water insured the application of a uniform temperature and rate of conduction. The bath temperatures were maintained within 1 C.

The degree of edema in both the injured and the uninjured feet in the experiments using cold as treatment was recorded as the increase in width of the feet in millimeters. In the experiments studying the effect of intravenous infusions on the rate of edema formation, a plethysmograph was used for greater accuracy.<sup>7</sup>

The blood plasma and lymph proteins were measured by the refractometer. The chemical measurements were made by standard analytic methods.

#### OBSERVATIONS

The effect of cold on the abnormal circulation of blood and lymph and on the rate of edema formation induced by a thermal burn was studied in the feet of dogs. The experiments are grouped according to which circulation was measured and into control groups testing the effects of the treatment bath and of a rapid intravenous infusion on edema formation.

*Effect of Cold on Lymph Circulation of the Burned Foot.*—The effect of cold on the increased flow and protein concentration of lymph from a burned foot of a dog was observed in three experiments (figs. 2, 3 and 4). In a previous publication<sup>8</sup> it was established that the minimal burn of a dog's foot producing a consistent rise in lymph flow and protein concentration was one caused by immersion in water at 70 C. for ten seconds. Such a minimal burn was chosen to test the response

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8. See article in this issue entitled "Threshold of Thermal Trauma and Influence of Adrenal Cortical and Posterior Pituitary Extracts on the Capillary and Chemical Changes: An Experimental Study," page 1015.

to therapeutic cold. The temperature selected for the cold bath was 10 C., based on the experience of Sir Thomas Lewis, who showed that the human skin survived, undamaged, immersion at this temperature.<sup>9</sup> (The absence of effect of this temperature on lymph flow and protein concentration in the dog is demonstrated in the control experiments described later.)

Under pentobarbital sodium anesthesia and without heparin infusion, the lymphatic vessels of both hind legs were cannulated. Control samples of lymph were collected after gentle massage and the size of the feet observed before the burning. In the first and second experiments both feet were burned and in the third only one. In the first experiment one foot was placed immediately after burning in the cold bath, where it was kept for three and a half hours. There was a slight spontaneous flow of lymph into the cannula while the foot was

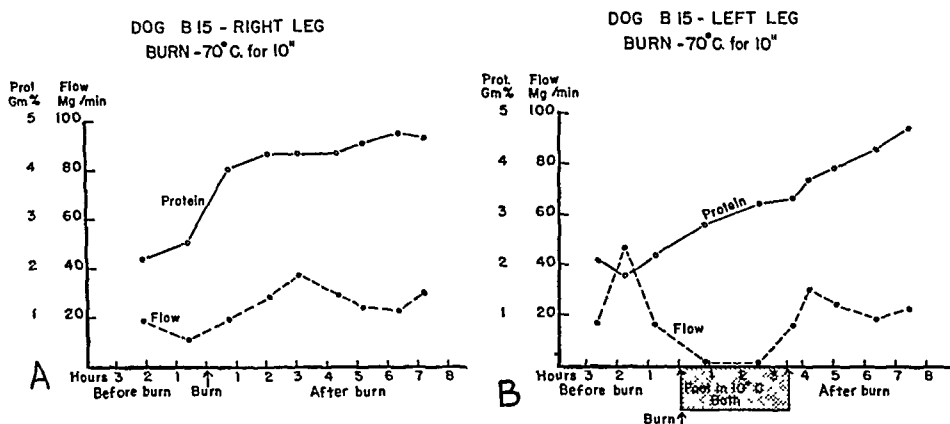


Fig. 2.—Effect of cold on lymph flow and protein concentration from a minimal burn of the hindfeet of dog B15. The burn was produced by immersion in water of 70 C. for ten seconds. *A*, the control leg; *B*, the cold-treated leg (10 C. for three and a half hours).

in the cold water, but on its removal from the cold to room atmosphere there was a prompt rise in flow (fig. 2*B*), comparable to that encountered soon after injury in the opposite, untreated leg (fig. 2*A*).

After injury the rise in protein concentration in the lymph from the foot burned but not treated with cold was prompt and in the concentration reached, 4.5 Gm. per hundred cubic centimeters, was typical of the change following a thermal injury of like severity (fig. 2*A*). The rise in protein concentration in the lymph from the treated foot was gradual. After withdrawal from the cold there was a further rise to the level of the untreated foot (fig. 2*B*).

9. Lewis, T.: Observations on Some Normal and Injurious Effects of Cold Upon the Skin and Underlying Tissues: I. Reactions to Cold, and Injury of Normal Skin, *Brit. M. J.* 2:795, 1941.

While the treated foot was in the cold bath, there was but barely visible swelling. After withdrawal, edema formed promptly, the size of the foot reaching that of the untreated foot within two hours. The untreated foot had swelled promptly after injury.

In the second experiment the foot was not immersed in the cold water until one and a quarter hours after the burn (fig. 3*B*). In the interval between burn and immersion, lymph flow, protein concentration and edema had increased comparably in both feet. After immersion in the cold, the flow of lymph was sharply reduced, but it did not cease while in the cold. The amount of edema, however, was visibly reduced by the end of the immersion in cold. On withdrawal of the foot from the cold the increased rate of lymph flow and edema formation was resumed. The protein concentration was reduced

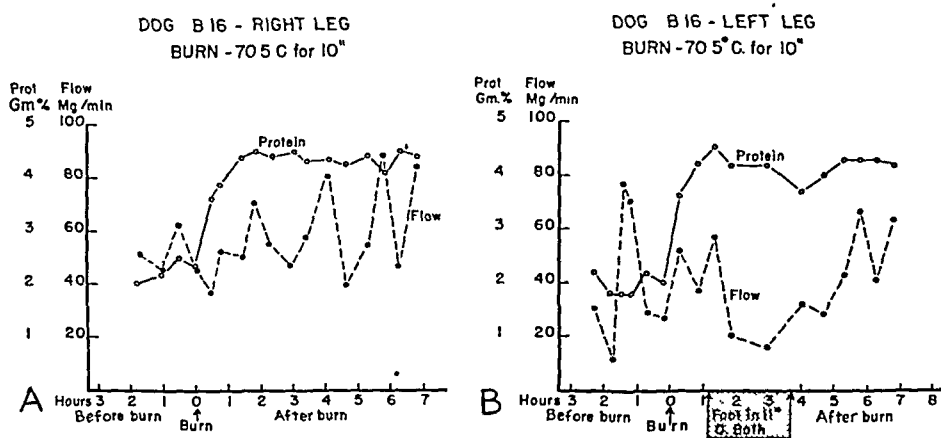


Fig. 3.—Effect of cold on lymph flowing from a minimal burn, 70.5 C. for ten seconds, in dog B16. The immersion in the cold bath (11 C.) was delayed until one and one quarter hours after burning. *A*, the control leg; *B*, the cold-treated leg.

slightly during immersion in cold and promptly rose again on withdrawal. The continued lymph flow during the immersion in this experiment was apparently in part at the expense of the edema fluid which had accumulated in the interval between injury and immersion in cold.

In the third experiment both a burned and an unburned foot were placed in the cold bath. The influence of the cold on the burned foot (fig. 4*A*) was comparable to that in the first experiment. There was no effect on the lymphatic circulation of the unburned foot produced by exposure for two hours and forty minutes (fig. 4*B*).

*Effect of Cold on Arterial and Lymph Circulation of the Burned Foot.*—In ten experiments both the arterial and the lymphatic circulations were measured.

The hematocrit value was measured at the time of heparinization. A control sample of lymph was obtained from the two feet. A period of stable blood flow for one to three hours was recorded. After the preburn width had been recorded, the hindfeet were burned in 4 dogs at 80 C., 5 at 90 C. and 1 at 100 C., all for fifteen seconds. Immediately after the burn, the hindfoot to be treated with cold was immersed in the water bath at 10 C., the immersion lasting for two and a half to six hours. The control hindfoot, hanging down from the table at the same level as the treated foot, was exposed to the room air. Neither the intensity of the burn nor the duration of the immersion in the cold bath altered the pattern of response. The findings in two typical experiments are given in figure 5.

A sequence of changes in the circulation of the skin and in the development of edema of the wound were visible as the result of the

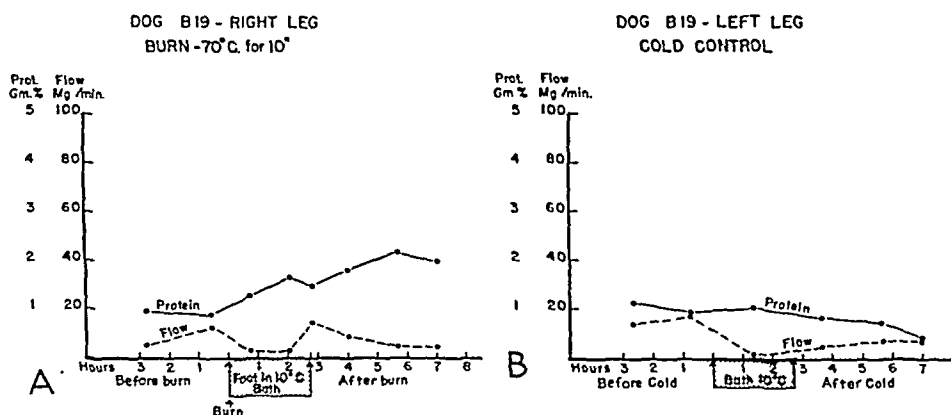


Fig. 4.—Comparison of effect of cold on the burned (A) and unburned foot (B) of dog B19. The burn was produced by an immersion at 70 C. for ten seconds and the chilling by a bath of 10 C. for two hours and forty minutes.

trauma and treatment. Immediately on immersion of the foot in the hot water, there was blanching, which was followed within a few seconds by a flush. On withdrawal, the flush of the untreated control foot continued, gradually changing to cyanosis. The foot swelled, and blebs formed between the toes.

The foot treated with the cold swelled but little and slowly while in the bath; no blebs appeared. On its withdrawal from the cold, the rate of edema formation was abruptly accelerated and blebs appeared (see bottom section of figure 5).

No consistent change in blood pressure, measured in the tibial artery, was noted as the immediate result of injury or therapy. In some experiments the pressure rose slightly on immersion of the foot in the hot water (fig. 5A); in others there was either a slight drop (fig. 5B) or no change. No changes were established as the result

of withdrawal from the hot water or of the immersion in cold. During the course of the experiment there were fluctuations in pressure in all animals, influenced by supplementary injections of pentobarbital sodium in some instances, and there was a general downward course of the pressure in some experiments (fig. 5*B*) and no change in others (fig. 5*A*). In all the experiments included, the condition of the animal

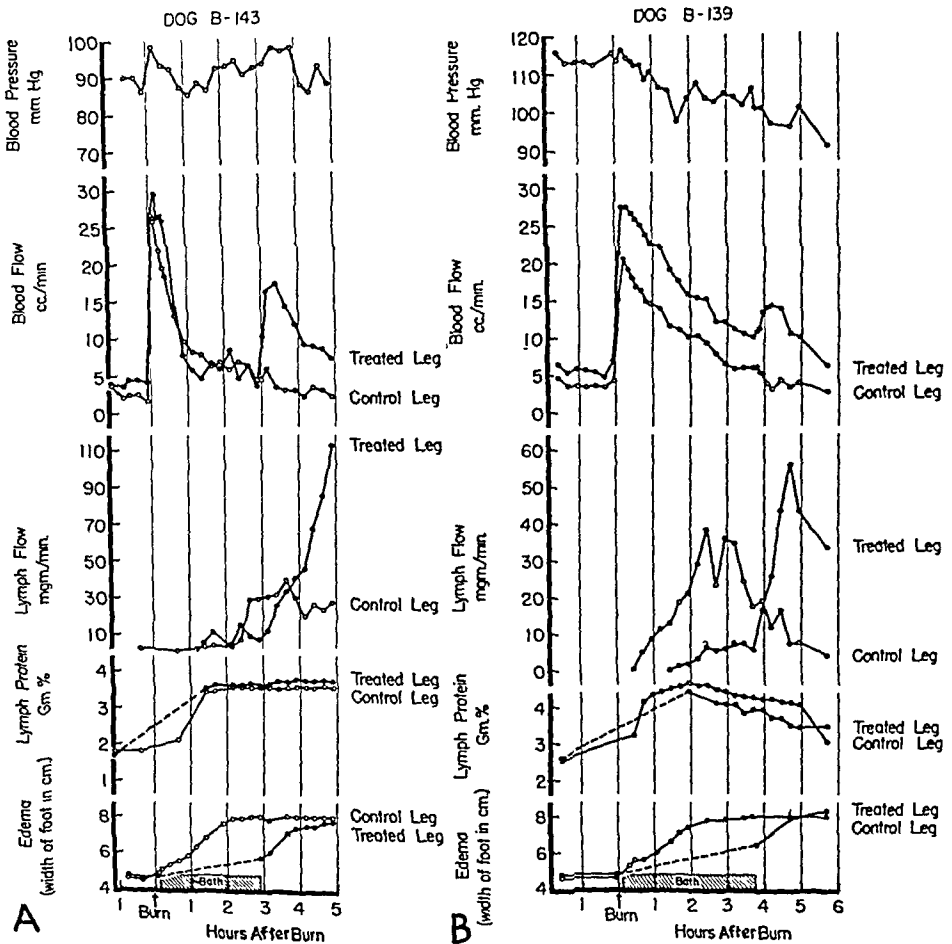


Fig. 5.—*A*, effect of a burn and cold treatment on the arterial and lymphatic circulation and edema formation in dog B143. The burn was produced by an immersion at 80 C. for fifteen seconds and the chilling by immersion at 10 C. for two and three quarters hours. The recorded blood pressure was measured by the tibial artery flowmeter. *B*, effect of a burn and cold treatment on the arterial and lymphatic circulations and edema formation in dog B139. The burn was at 90 C. for fifteen seconds and the chilling at 10 C. for three and three quarters hours. The recorded blood pressure was of the tibial artery.

was considered satisfactory, blood flow being maintained and the arterial pressure at no time below 85 mm. of mercury.

Striking alterations of blood flow were consistently encountered immediately after the burn and in the treated foot after withdrawal

from the cold bath. In all experiments there was an abrupt immediate rise in flow when the feet were immersed in the hot water, the extent of the rise being independent of the temperature within the range of temperature used. Removal from the water was followed by a fall in flow, abrupt initially in some experiments and gradual in others. This fall was not influenced by the immersion in cold water. In the untreated leg the flow returned to the preburn rate in three to four hours.

In the treated leg there was a second abrupt rise in flow on withdrawal from the cold bath. This rise was not to as high a level as that reached immediately after the burn, but it was sustained for from forty minutes to one and a half hours. Thereafter the flow declined to the preburn level. In the foot not exposed to cold there was no consistent change in flow at the time when the treated foot was removed from the cold bath. In some experiments there was either a slight fall, a rise or no recognizable change. This difference in flow pattern of the two feet on cessation of cold therapy indicated that the second rise in rate of flow in the treated leg is the result of a reflex, locally governed.

The pattern of flow and protein concentration of lymph from the burned foot immersed in the cold bath was comparable to that of the first group of experiments. During the exposure to cold, the flow of lymph and the development of edema were retarded. The more severe the injury, the more exaggerated the difference in flow between the treated and the control foot. On removal from the cold bath, the rate of flow increased rapidly and subsequently decreased when the edema of the treated foot had reached its maximum, an amount comparable to that of the control foot, which had been reached two hours after injury (fig. 5).

The rise in protein concentration in the lymph of the control foot was typical of that following thermal trauma. The protein concentration also rose in the lymph from the treated foot during the application of the cold. As soon as the volume of lymph was sufficient for measurement, in some experiments the concentration was found already to have reached or exceeded that of the lymph from the control foot. In other experiments the concentration in the lymph from the treated foot remained below that in the lymph from the control foot throughout the period of exposure to cold.

It is to be noted at this point that the pattern of lymph flow is altered by the cold throughout the period of immersion of the foot; in contrast, the arterial blood flow is not influenced until removal of the foot from the cold, and then only is the blood flow different in the two feet.



In conformity with the previously reported observations, the lymph in the initial period after a burn at 90 or 100 C. showed slight hemolysis.

In the burned foot not immersed in the cold bath the maximum edema is reached two to two and a half hours after the burn. In the treated foot the rate of edema formation is much lower than in the control foot, but it is not negligible during the period of treatment. This rate is not consistent in all experiments. In the period immediately following withdrawal from the cold bath there is a prompt increase in the rate of edema formation. In experiments in which the bath was continued for only three to four hours, the edema eventually reached the volume present in the control feet. In the experiment in which immersion lasted for six hours, edema ceased to form before the size of the foot reached that of the control foot while in the bath. After withdrawal, although the edema increased a little, the size never reached that of the control foot.

*Effect of Cold on Lymph Circulation of the Unburned Foot.*—Because it was observed in the first group of experiments that the flow and the protein concentration of the lymph from an unburned foot were unaltered by an immersion at 10 C. for two hours and forty minutes (fig. 4B), it was considered wise to test at a lower temperature to make sure that the immersion itself did not damage the capillary bed.

After cannulation of the lymphatic trunk, one foot of each of two animals was immersed for three and three and three-quarter hours, respectively, in water at 0 C. and the lymph flow and protein concentration observed for several hours thereafter (fig. 6A and B). In the experiment with the immersion lasting for three hours (fig. 6A), there was initially no flow, but after immersion there was a moderate spontaneous flow that was still rising when the experiment was ended. The protein concentration after immersion was nearly one gram lower than during the period of massage before immersion. In the experiment with the immersion lasting three and three-quarter hours (fig. 6B) there was a slight spontaneous flow after removal from the bath and, as in the previous experiment, a fall in protein concentration. The failure of the protein concentration to rise excluded a bath of this temperature and duration as the cause of any of the changes recorded in the experiments on treatment.

*Effect of Intravenous Infusion.*—The effect of a rapid intravenous infusion of isotonic sodium chloride and sodium lactate solutions on rate and degree of edema formation was studied in four experiments. The volume of the four feet of each animal was measured in separate plethysmometers. One forefoot and one hindfoot were burned at 90 C. for fifteen seconds, a burn of medium severity known to produce a consistent curve of edema formation with minimal loss of elasticity

of the skin. Experience has indicated that nearly maximum edema is produced by such a burn, the peak of the edema having been reached between the second and third hours after injury.

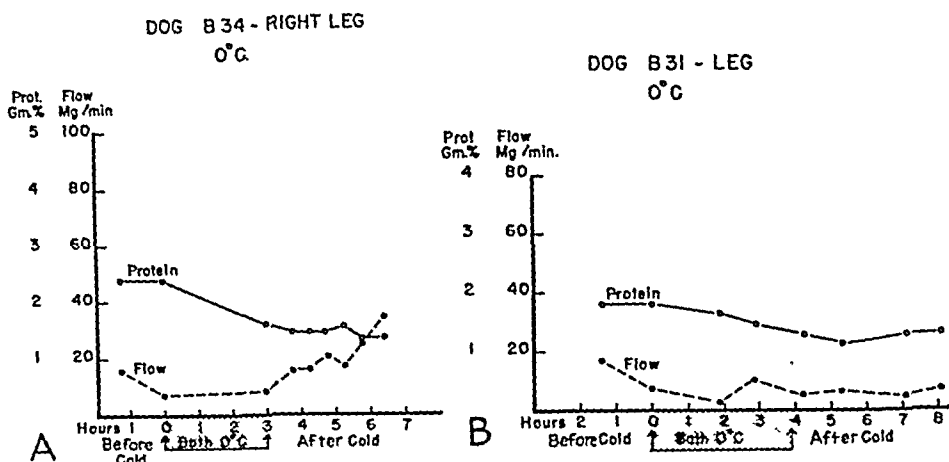


Fig. 6.—*A*, effect of cold on the flow and protein concentration of lymph in right leg of dog B34. The immersion at 0 C. for three hours was followed by an increase in flow but not of protein concentration. *B*, effect of cold on the flow and protein concentration of lymph in right leg of dog B31. The immersion at 0 C. for three hours was followed by slight spontaneous flow and a gradual fall in protein concentration.

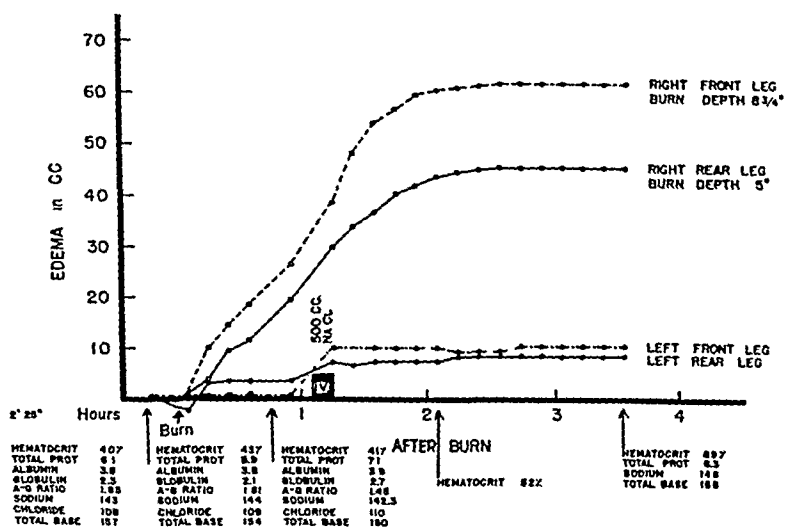


Fig. 7.—Effect of intravenous infusion on rate and degree of edema formation following a burn at 90 C. for fifteen seconds in dog B121. Infusion of 500 cc. of isotonic sodium chloride was begun seventy minutes after injury. There was a rise in the rate of edema formation in the burned feet as well as a slight increase in the volumes of the uninjured feet.

In the first experiment an infusion of 500 cc. of sodium chloride was given in a twelve minute period starting at the seventieth minute

after the burn. An increase in the rate of edema formation in the injured feet was apparent immediately after the infusion (fig. 7). There was also a slight increase in the volumes in the uninjured feet, which indicated an expansion of the entire extracellular space.

In a second experiment the infusion of 400 cc. of isotonic sodium lactate solution was not started until the end of the fourth hour after the burn and one hour after the volume of edema had ceased to increase in both injured feet. Immediately after the infusion there was a slight further distention of the wounds. No significant increase in the volume of the uninjured feet was observed (fig. 8). The other two experiments showed similar effects.

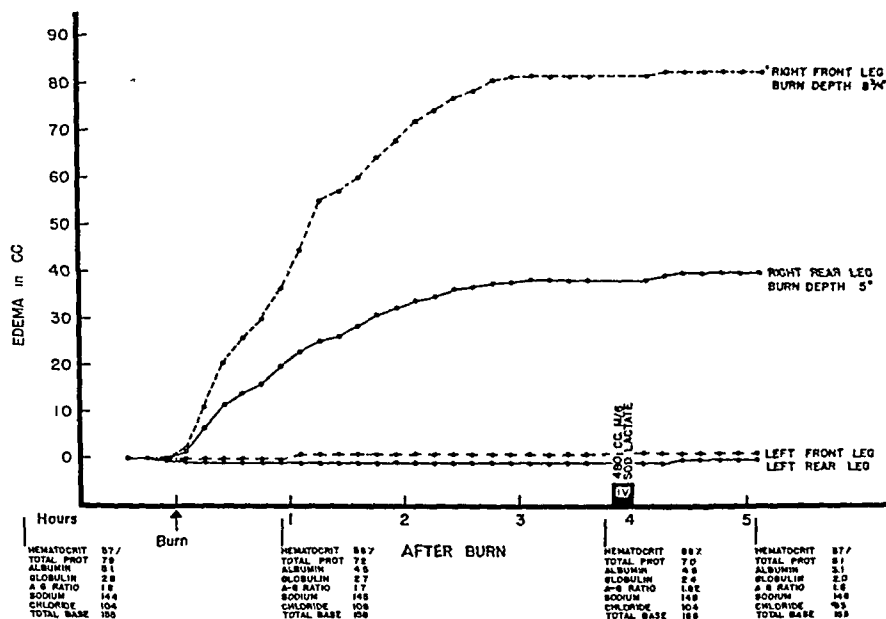


Fig. 8.—Effect of intravenous infusions on rate and degree of edema formation following a burn at 90 C. for fifteen seconds in dog B122. Infusion of 400 cc. of isotonic sodium lactate was begun four hours after injury. There was slight further increase in edema of the burned feet but no significant change in the volumes of the uninjured feet.

The hematocrit value, serum total protein, albumin-globulin ratio, sodium content, chloride content and total base were measured before and after injury and before and after the infusion. The changes observed were consistent with hemoconcentration following the burn and hemodilution following infusion (figs. 7 and 8).

#### COMMENT

It is true that the application of cold to a burn wound diminishes the rate of edema formation and therefore the rate of loss of plasma volume and that it may even diminish slightly the volume of edema

which has already formed before its application, but it is not necessarily true that cold is a treatment of choice for the burned patient.

Cold retards the loss of plasma volume but does not eliminate it. The wound volume slowly increases while the chilling continues, and though the volume reached may be less than that expected had the wound not been chilled, our experiments do not indicate a sparing of plasma volume adequate to indicate the use of cold on this basis. The sparing of plasma loss is also not a problem in a patient with a circumscribed burn but is most needed in the extensively burned patient. If sufficient cold is applied for a therapeutic effect to an extensive burn of the body surface, it will cause a drop in body temperature. Experiments using cold not cited in the observations of this paper were carried out on dogs with all four legs of each burned; there was such a drop in body temperature that survival was threatened.

It is reasonable to conclude that cold may retard the development of infection and diminish damage due to an impaired circulation, but cold also reduces the rate of the healing processes. Tempting though it may be to use cold in the therapy of burns, it must be recognized that an excessive use of cold, with either too severe a cooling application or too long an exposure, may in itself result in tissue damage. Until more is known of the critical temperature and period of exposure which can be employed with safety, it is considered wise to limit the use of cold to the temporary alleviation of the pain of burns of small extent. In this act it may be extremely useful.

#### SUMMARY

The effect of a cold water bath on the abnormal circulation of blood and lymph and on the rate of edema formation induced by a thermal burn was studied. The temperature selected for the cold bath was 10 C., inasmuch as this degree of cooling in itself has been shown to cause no damaging effect on tissues.

Exposure to cold alters the pattern of lymph flow and protein concentration. Lymph flow from a burned foot is sharply reduced during the entire period of immersion in the cold bath, regardless of whether cold is applied immediately after the burn or at some interval later. The rise in protein concentration of lymph and in rate of edema formation is also retarded. These changes occur apparently as a result of shunting of blood flow away from the damaged capillaries. On withdrawal of the foot from the cold, the rate of lymph flow and edema formation is accelerated and the rise in protein concentration of lymph resumed until it reaches or even exceeds the levels of the untreated foot.

Cold does not alter the pattern of arterial blood flow in the burned foot until removal of the foot from the cold bath is effected. This is in contrast to the pattern of lymph flow, which is strikingly altered only during the period of immersion in the cold. When exposure to cold ceases, there is an immediate rise in blood flow in the treated foot but no striking or consistent change in the untreated foot. This difference in flow pattern in the two feet indicates that the rise in blood flow in the treated foot is the result of a reflex locally governed.

Neither the intensity of the burn nor the duration of immersion in the cold bath altered the pattern of response in the lymphatic or arterial circulation. No consistent changes in blood pressure were established during infliction of the thermal injury, in the period immediately following injury or during therapy with cold.

The limitations of the use of cold in the therapy of burns are analyzed and discussed.

# CIRCULATION OF THE BLOOD AND LYMPH IN FROST-BITE AND INFLUENCE OF THERAPEUTIC COLD AND WARMTH

An Experimental Study

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**F**ROSTBITE is a common injury of man transposed from temperate to cold climate, yet little is known of the physiologic disturbances it creates, and the treatment of it is still in the realm of empiricism. The adverse effects of this injury assumed special importance during the recent war, when these studies were undertaken.

The resemblance of frostbite to burns, the experimental observations of Lewis<sup>1</sup> and the experience in the early years of World War II in the treatment of immersion foot with cold<sup>2</sup> suggested that the disorder of the arterial and lymphatic circulation induced by frostbite might well be similar to that following burns. Accordingly, as a beginning to a better physiologic understanding and more rational therapy, the experimental studies of the circulatory disturbances of trauma due to burns were extended to frostbite, including the possible use of cold and warmth in treatment.

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From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. Lewis, T.: Observations on Some Normal and Injurious Effects of Cold Upon the Skin and Underlying Tissues: I. Reactions to Cold, and Injury of Normal Skin, *Brit. M. J.* **2**:795, 1941; II. Chilblains and Allied Conditions, *ibid.* **2**:837, 1941; III. Frostbite, *ibid.* **2**:869, 1941.

2. Webster, D. R.; Woolhouse, F. M., and Johnston, J. L.: Immersion Foot, *J. Bone & Joint Surg.* **24**:785, 1942. White, J. C., and Scoville, W. B.: Trench Foot and Immersion Foot, *New England J. Med.* **232**:415, 1945.

## METHODS

Frostbite was produced experimentally by immersing the dog's foot in a liquid mixture of ethyl alcohol and solid carbon dioxide. Different degrees of tissue injury were produced by varying the temperature of the cooling mixture and the duration of the immersion. The desired temperatures of the immersion bath were obtained by changing the proportion of the two components with constant stirring.

The animal was anesthetized and prepared in a manner similar to that used in the studies of experimental thermal burns treated with cold (see previous paper). Under aseptic precautions the lymphatic trunks of both hindlegs were cannulated above the ankle; the circulating blood was heparinized.<sup>3</sup> The anterior tibial arteries were cannulated and attached to calibrated flowmeters and blood pressure manometers. A carotid artery was cannulated and the pressure within it recorded. After a period of stable blood flow had been assured, the hindfeet were immersed in the freezing mixture and the changes in the arterial and lymphatic circulations observed.

## OBSERVATIONS

The circulatory pattern of frostbite of varying severity in the foot of the dog has been defined and the effect of both cold and warmth on it determined in twenty-seven experiments. In addition to the arterial and lymphatic flows, the edema formation, with its magnitude and composition, has been measured. The course of events in experiments involving frostbite of moderate severity is presented first, followed by the results of those illustrating minimal and severe frostbite. Experiments evaluating the effect of continued blood flow in mitigating the degree of frostbite and determining the use of varying temperatures as therapy are described in the subsequent sections.

## CIRCULATORY PATTERN OF FROSTBITE

*Moderate Frostbite.*—With the dog under pentobarbital sodium anesthesia, the lymphatic vessels of both hindlegs cannulated, the blood heparinized, a flowmeter in each anterior tibial artery and the carotid blood pressure cannula recording, the effect of frostbite was examined. Before immersion in the freezing mixture a control hematocrit reading was taken at the time of heparinization. A period of stable blood flow was observed for one hour or longer. Control samples of lymph were obtained by gentle massage, there being no demonstrable spontaneous lymph flow in the resting uninjured extremity. The width of both feet was measured as a base line for judging edema formation. Frostbite of one foot was produced at a temperature of minus 18 C. for twenty minutes in one experiment and thirty minutes in another; the other foot in both experiments was kept as a control (chart 1).

On immersion in the freezing mixture, the foot blanches slowly over a period of two minutes, freezes gradually from the skin inward

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3. The heparin (liquaemin®) was supplied through the generosity of Roche Organon, Inc., of Nutley, N. J.

and on removal is frozen solid. A flush rapidly appears three to four minutes after removal from the freezing mixture. Thawing of the frozen tissue starts both proximally and distally, the midportion being the last to thaw. Visible edema follows the thawing, and the foot assumes initially the shape of a dumbbell. The red color of the initial flush yields gradually to a cyanotic hue. Blebbing between the toes and

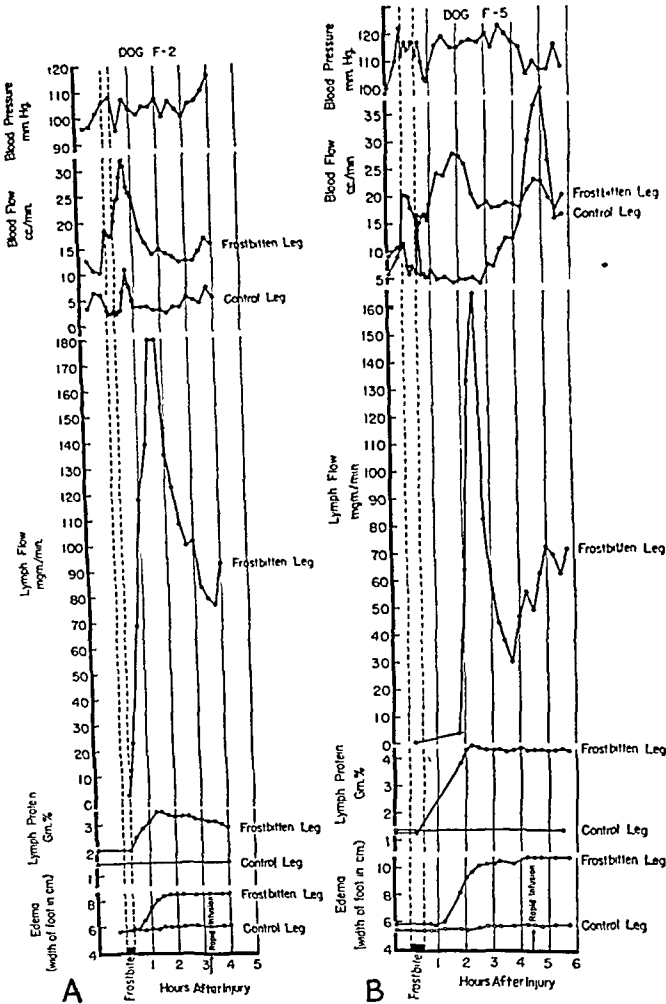


Chart 1.—*A*, effect of moderate frostbite on arterial and lymphatic circulation and on edema formation. *A*, frostbite was produced by immersion of one hindfoot in a bath of minus 18 C. for twenty minutes, the other foot being used as a control. *B*, frostbite was produced by immersion of one hindfoot in a bath of minus 18 C. for thirty minutes, the other foot being used as a control.

a generalized outpouring of exudate comparable to those following a burn appear. No changes were visible in the control foot.

The changes in arterial blood pressure were consistent only in the period immediately following withdrawal of the foot from the freezing mixture. While the foot was being immersed the response in blood pressure varied. In some of the experiments there was a slight rise



(chart 1 *B*); in others (not depicted) there was a slight fall or no change. During the period of immersion, however, there was usually no change although in some of the experiments there was a slow slight fall. On withdrawal of the foot there was an immediate decisive fall in pressure in all experiments. From this fall there was a gradual recovery to the level at the time of immersion, manifest in twenty to thirty minutes but usually not complete for an hour. Subsequent changes were dependent on the circulating volume, the effect of the reinfusions and anesthesia.

The mean arterial pressures recorded by the manometer connected with the flowmeters and the cannula in the carotid artery were essentially identical in all experiments; therefore, only the carotid pressure is depicted in the charts.

On immersion of the foot in the freezing mixture the blood flow rose in some experiments but did not change in others. Throughout the immersion there was a progressive decrease in flow. In the experiment with the twenty minute immersion this decline was slight (chart 1 *A*); in that with the thirty minute immersion it was greater (chart 1 *B*). The amount of decrease in flow was proportionate to the severity of the freezing. After removal, not immediately but with thawing, there was an increase in flow. No decrease in flow was noted with the fall in blood pressure occurring immediately after withdrawal. When thawing was advanced, and at the time of the rise in blood pressure, there was a further increase in blood flow. The maximal blood flow was reached at the peak of the blood pressure rise in one experiment (chart 1 *A*) but not until twenty minutes after the peak in another (chart 1 *B*).

The blood flow in the control foot changed but little and inconsistently on the initiation of the trauma to the opposite foot. Throughout the period of immersion of the other foot, there was no change in flow. On withdrawal of the injured foot there was a prompt sharp rise in the rate of flow, which was usually transient as compared to that in the traumatized foot.

In the frostbitten foot there was invariably an increase in flow and protein concentration of the lymph comparable to that following a burn and indicating increased capillary filtration. The onset of the flow of abnormal lymph was delayed by the freezing, an acceleration occurring with the thawing. Thus in the experiment with but twenty minute immersion the onset of spontaneous flow occurred immediately after withdrawal and the rate of flow reached its maximum in one hour and ten minutes after withdrawal (chart 1 *A*); in the experiment with longer immersion, thirty minutes, spontaneous flow was not established until an hour after withdrawal, and the rate had not reached its maximum until nearly two hours after withdrawal (chart 1 *B*).

The rise in lymph flow lagged behind that of the blood flow and reached its peak at the time of maximum edema. The peak was short lived and was followed by a decline, nearly as rapid as the preceding rise. The initial decline, however, lasted but one hour, did not fall to zero and was followed by a fluctuating flow.

The protein concentration of the lymph from the frostbitten foot rose with the onset of spontaneous flow to levels comparable to those following burns. In the moderate frostbite the protein concentration rose from 2.0 to 3.6 Gm. per hundred cubic centimeters (chart 1 *A*) and in the more severe frostbite from 1.3 to 4.4 Gm. The pink tinge of hemolysis was evident in the lymph immediately after thawing; its occurrence was transient.

In the control foot there was no spontaneous lymph flow and either no change or a slight rise in protein concentration but no more than that expected as a result of the continued massage needed to secure the samples.

Edema followed on the heel of thawing; its formation was rapid in feet frostbitten to this degree. After immersion for twenty minutes, the foot thawed quickly; edema was apparent in thirty minutes, and its peak was reached seventy minutes after withdrawal from the cold bath (chart 1 *A*). In the experiment with the thirty minute immersion edema formation was not evident until one hour after withdrawal and did not reach its peak until two hours after withdrawal from the bath (chart 1 *B*).

*Minimal Frostbite.*—Under experimental conditions identical with those described in the first section, one foot of a dog was immersed for fifteen minutes in a freezing mixture at a temperature starting at minus 5 C. and falling to minus 8 C. Blanching of the immersed foot was visible, but the tissues were not rigid on withdrawal. After withdrawal a flush immediately appeared.

The blood pressure changes were comparable to those recorded in the dog with the moderate frostbite (see chart 2 *A* and chart 1). The blood flow in the traumatized foot in the present experiment (chart 2 *A*) increased during the immersion, in contrast to the fall in that with the more severe frostbite accompanied with a freezing of the tissues (charts 2 *A* and 1 *B*). There was no increase in flow after withdrawal. The changes in flow encountered in the control foot were like those of the frostbitten foot.

The changes encountered in the lymphatic circulation indicated minimal damage to the capillaries of the frostbitten foot. There was a slight spontaneous flow immediately after the immersion, but two hours later the sample of lymph had to be obtained by massage. There was, however, a sharp rise in protein concentration after the immersion,

which was not seen in the control leg and therefore signified alteration in capillary permeability. No evidence of hemolysis was apparent in the lymph. (The lymph in the control foot was obtained only by massage.)

There was slight progressive edema formation, but it was no greater in the immersed foot than in the control foot. The edema was adjudged

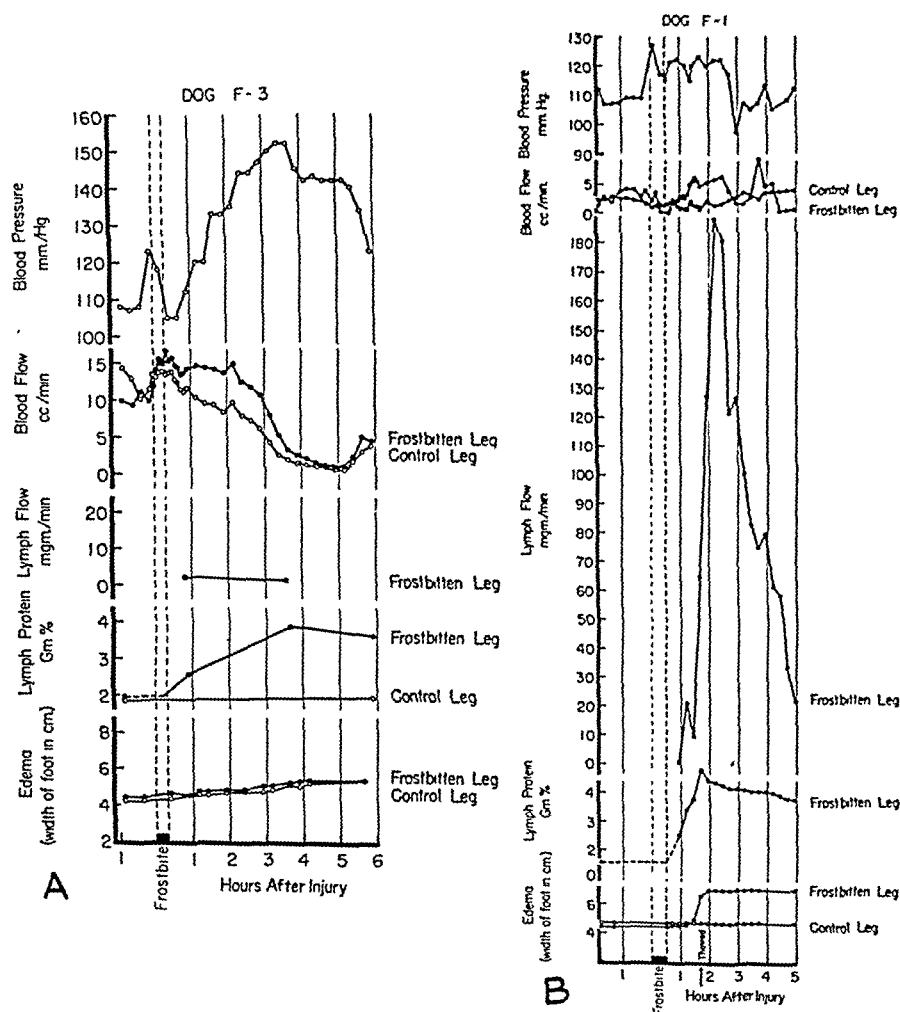


Chart 2.—*A*, effect of minimal frostbite on arterial and lymphatic circulation and on edema formation. Frostbite was produced by immersion of one hindfoot in a bath of minus 5 to minus 8 C. for fifteen minutes, the other foot being used as a control. *B*, effect of severe frostbite on arterial and lymphatic circulation and on edema formation. Frostbite was produced by immersion of one hindfoot in a bath of minus 25 C. for thirty minutes.

to be presumably the result of the dependency of the feet during the experiment.

The increase in protein concentration of the lymph and the length of the period of spontaneous lymph flow point to a damage as the result of the immersion in the cold bath. The absence of greater edema in the

immersed foot and the shortness of the period of spontaneous flow of lymph indicate that the damage from frostbite was minimal.

*Severe Frostbite.*—Immersion of the dog's foot in a freezing mixture at minus 25 C. for thirty minutes resulted in a severe frostbite (chart 2 *B*). During immersion the foot froze rigidly, and it took one and three quarter hours to thaw completely. The blood pressure changes were comparable to those encountered in the previous experiments. The blood flow fell to zero during the period of immersion. With thawing, the increase in flow was slow, and thereafter the flow was irregular. The high peak of flow seen after the less severe frostbites was absent. In the lymphatic circulation there was a delay in the increase of flow and protein concentration during thawing. Evidence of hemolysis was present in the initial post-traumatic samples of lymph. The rate of edema formation was rapid after thawing. These changes in the lymph flow and protein concentration were comparable to those following a severe burn.

*Effect of Interruption of Blood Flow on Degree of Frostbite.*—Because of the decrease in blood flow encountered during immersion in cold and the cessation of flow with freezing, an attempt was made to evaluate the relationship of the reduction of blood flow introduced by the blood flow cannula to the degree of frostbite. The transitory ischemia occurring during cannulation had already been controlled in each experiment in the foot not frostbitten; no evidence of increased capillary permeability was observed.

During the period of immersion of both feet, the arterial circulation of one foot was interrupted by clamping the exposed anterior tibial artery. A frostbite of moderate degree was chosen—immersion for twenty-five minutes at a temperature starting at minus 18 C. and descending to minus 20 C. The changes in lymph flow and protein concentration and the increase in edema in the frostbitten, nonischemic foot were typical of those following the frostbite in the previous experiment (chart 3 *A*). In the foot rendered ischemic during immersion there was evidence of greater damage. Freezing of the immersed tissues was grossly complete and the period of thawing prolonged. After the thawing, the greater rise in lymph flow and protein concentration and the more promptly appearing and increased volume of edema indicated greater damage during freezing. The greater damage in the ischemic foot is believed to be due more to the absence of the warming effect of circulating blood than to the anoxia of ischemia.

#### THErapy IN FROSTBITE

The assay of the effect of cold on experimental frostbite was indicated not only because of a recommendation of its use in the therapy

of frostbite in the human being but also to test further the apparent similarity of the circulatory changes of thermal burn and frostbite.

*Cold in the Therapy of Frostbite.*—The effect of cold water therapy, at 10 C., on the abnormal arterial and lymphatic circulation and on the development of edema following frostbite was explored in three experiments. The findings in a typical experiment are shown in chart 3 *B*.

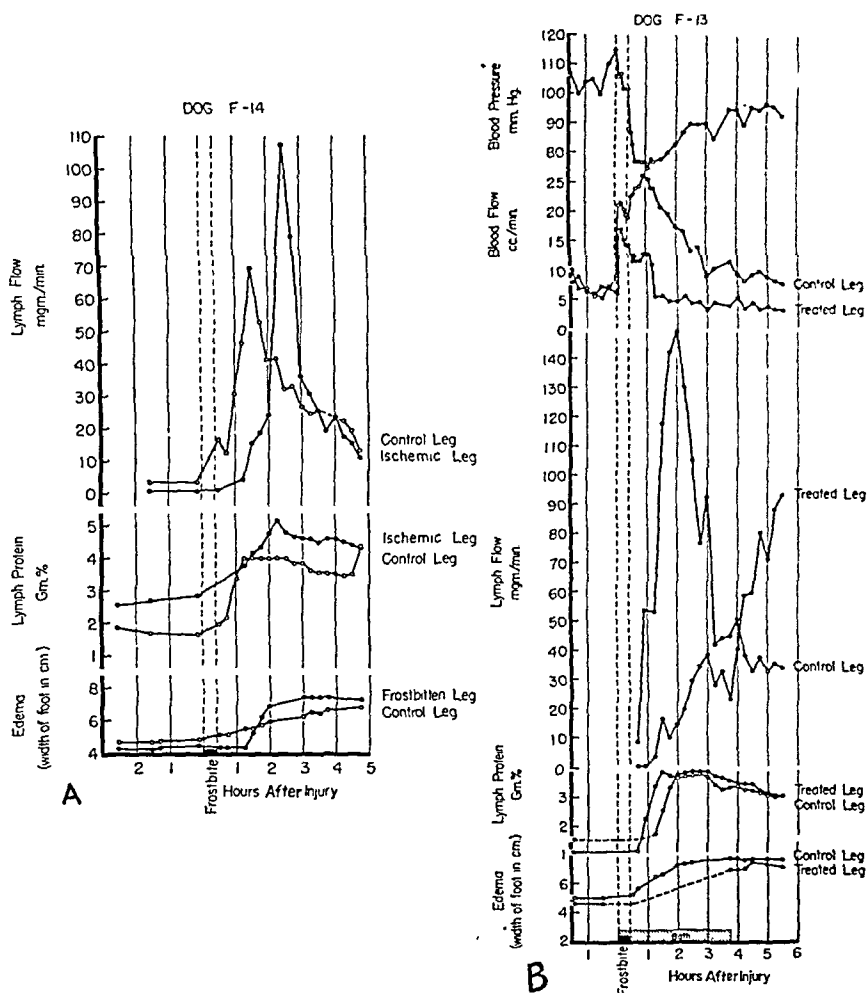


Chart 3.—*A*, effect of ischemia on degree of frostbite. Moderate frostbite was produced by immersion of both hindfeet in a bath of minus 18 to minus 20 C. for twenty-five minutes. During the period of immersion, the arterial circulation of one hindfoot was interrupted by clamping the exposed anterior tibial artery; the other foot was used as a control. *B*, effect of treatment with cold on the abnormal arterial and lymphatic circulation and the development of edema following frostbite. Moderate frostbite of both hindfeet was produced by immersion in a bath of minus 18 to minus 20 C. for twenty-five minutes, and one of the frostbitten feet was then immersed in the treatment bath of 10 C. for three and three-quarter hours.

The reasons for the use of 10 C. are recounted in the previous paper ("The Effect of Therapeutic Cold on the Circulation of Blood and

Lymph in Thermal Burns"). The same experimental method was employed. The frostbite was that of moderate degree, a 25 minute immersion in a freezing mixture of minus 18 C. to minus 20 C. One of the two frostbitten feet was immersed in the bath of 10 C. immediately after freezing; the period of this therapeutic immersion varied from three and one-quarter to three and three-quarter hours. The frostbite produced the typical changes already described.

The blood flow to the treated and untreated feet was not significantly dissimilar. In the experiment charted, the blood flow to the treated foot was lower than that to the control foot even during the period of immersion.

The lymph flow from the treated foot was retarded throughout the period of treatment with cold. Immediately after its removal from the treatment bath, there was a sharp increase in flow, which reached a level higher than that from the control foot. The rise in concentration of lymph protein was also retarded, the final concentration reached being the same as that from the control foot.

The edema formation was also apparently slightly delayed by the treatment in the cold bath.

The delay in increase of lymphatic flow during immersion in the treatment bath and the prompt increase following removal from the bath indicate a local restraining mechanism comparable to that encountered in burns treated with cold.

*Treatment of Frostbite with Warmth.*—The therapeutic effect of a warm water bath, at 40 C., on frostbite was tried in five experiments. Before the inducement of frostbite, the effect of 40 C. was explored in one experiment. A ten minute immersion at this temperature produced a slight flush of the immersed foot but no change in the arterial inflow, lymph flow or protein concentration. The frostbite was produced by immersion at minus 18 C. for twenty-five minutes. After the frostbite one foot was immersed in the warm bath for periods varying from two and three-quarter to three and a half hours.

No significant differences were observed in the blood flow to the warmed foot as compared with that to the untreated foot. The lymph flow and protein concentration of the treated foot increased more promptly than those of the untreated foot. Consistent significant differences in the maximal protein concentrations of the lymph from the two feet were not noted. The concentration rose more slowly in the warmed feet. Evidence of hemolysis disappeared more rapidly from the lymph of the warmed feet.

The experience with these five experiments suggests that the differences in the behavior of the lymphatic circulation of the two feet are to be explained by the faster thawing of the foot placed in the warm bath.

## COMMENT

We have examined experimentally the disorder of arterial and lymphatic circulation induced by frostbite. The abnormalities found are strikingly similar to those following a hot water burn. There is the same evidence of increased arterial blood flow, damaged capillary membranes and overloaded lymphatic trunks. The only major dissimilarity arises from the fixation of tissues when frozen; blood flow is reduced and even arrested if the freezing is deep. It is not until the tissues thaw that the circulatory pattern encountered after thermal trauma manifests itself.

The similarity of the circulatory disorder between frostbite and burns is seen in many of the details. The shunting of blood from the damaged capillaries as a result of treatment with cold water at 10 C. occurs after both types of injury. Blood flow, augmented by the injury, is not reduced by the treatment with cold, whereas both the lymph flow and the edema formation are restrained. That this apparent shunting of blood is controlled by a local reflex in both types of injury is suggested by the observation that the restraint of lymph flow and edema formation is not seen in the contralateral damaged but untreated foot.

Those who feel that edema is deleterious to a wound may be tempted to use cold in their therapy of frostbite. As in the treatment of burns, we are fearful lest prolonged exposure to even such a mild degree of cold as immersion in water at 10 C. would in itself lead to tissue injury.

Except for the acceleration of thawing which it induces, warmth used in treatment does not alter the pattern of circulatory disorder. There is no evidence that a shortening of the length of time the tissues stay frozen decreases or alters the nature of the injury to the cells. We therefore have obtained no evidence pointing to benefit from the use of warmth in the treatment of frostbite.

## SUMMARY

Frostbite was produced experimentally by immersing the dog's foot in a liquid mixture of ethyl alcohol and solid carbon dioxide. Different degrees of tissue injury were obtained by varying the temperature of the cooling mixture and the duration of immersion. We have found that varying the degree of injury modifies the physiologic phenomena of frostbite but does not basically alter it.

The disordered arterial and lymphatic circulation induced by frostbite was examined. During the period of freezing, blood flow progressively decreases in proportion to the severity of injury; not until thawing begins does blood flow to the injured extremity increase. From the frostbitten foot there is invariably an increase in lymph flow and protein concentration comparable to that following a burn; the

onset of flow of abnormal lymph is delayed by freezing and greatly accelerated with thawing. The rise in lymph flow lags behind that of blood flow and reaches its peak at the time of maximum edema. The protein concentration of the lymph rises with the onset of spontaneous flow to levels comparable to those following a burn.

The effects of cold (10 C.) and warmth (40 C.) used as therapy on the abnormal arterial and lymphatic circulation of frostbite and the development of edema were investigated. No significant differences were found in the blood flow of the treated and untreated feet. In the therapy with cold, lymph flow from the treated foot as well as lymph protein concentration and edema formation is retarded. When warmth was used as treatment, the lymph flow and protein concentration of the treated foot increased more promptly than those of the untreated foot. Consistent significant differences in the maximal protein concentrations of the lymph from the two feet were not noted.

The significance of these observations is discussed.



# EXPLORATIONS INTO THE PHYSIOLOGIC BASIS FOR THE THERAPEUTIC USE OF RESTRICTIVE BANDAGES IN THERMAL TRAUMA

An Experimental Study

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**E**NTHUSIASTIC recommendations of the use of pressure dressings and plaster casts in the local treatment of burns have appeared from a number of clinics.<sup>1</sup> Pressure dressings are advised because they tend to limit swelling of the wound, while plaster casts, if applied immediately after injury, prevent swelling.<sup>1c</sup> Although nearly all authors agree that such restrictive dressings are beneficial to wound healing, they have been advocated for a variety of reasons. Allen and Koch<sup>1a</sup> hold that an occlusive pressure dressing restores the tissue pressure normally dependent on an intact integument and thus aids in the return of venous blood. They cited Blair<sup>2</sup> as pointing out that pressure

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From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

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1. (a) Allen, H. S., and Koch, S. L.: The Treatment of Patients with Severe Burns, *Surg., Gynec. & Obst.* **74**:914, 1942. (b) Siler, V. E., and Reid, M. R.: Symposium on Burns: Clinical and Experimental Studies with the Koch Method of Treatment of Heat Burns, *Ann. Surg.* **115**:1106, 1942. (c) Glenn, W. W. L.; Gilbert, H. H., and Drinker, C. K.: The Treatment of Burns by the Closed Plaster Method, with Certain Physiological Considerations Implicit in the Success of this Technique, *J. Clin. Investigation* **22**:609, 1943. (d) Levenson, S., and Lund, C. C.: The Treatment of Burns of the Extremities with Close Fitting Plaster of Paris Casts, *J. A. M. A.* **123**:272 (Oct. 2) 1943. (e) Sellers, E. A., and Willard, J. W.: The Effect of Plaster Bandages and Local Cooling on Haemoconcentration and Mortality Rate in Burns, *Canad. M. A. J.* **49**:461, 1943. (f) Alrich, E. M., and Lehman, E. P.: Studies on Burns: I. Effect of Plaster Confinement Applied at Varying Intervals after Burning, *Surgery* **15**:899, 1944.

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limits both venous and lymph stasis. Noticing that the dressings promote comfort and that the wounds showed minimal infection, Siler and Reid <sup>1b</sup> recommended pressure because it tends to prevent the loss of plasma from the circulation, a point on which Koch and others agree.

As far back as 1924 Blair used mechanical pressure on wounds because it limited "the amount of plastic material that pours into the wound," <sup>2</sup> a point which Drinker and his collaborators <sup>1c</sup> have emphasized recently in more finite protein terms. They pointed out that not only does plasma pour out of the circulation through the dilated and permeable capillaries into the wound but also that the proteins of the plasma eventually become coagulated in the interstices of the stretched wound. They stressed the fact that not only must these proteins eventually be redissolved during healing but that the coagulum may serve as a nidus for infection and lead to increased fibrosis and scarring. They also expressed the belief that stretching by edema tears the tissues and leads to scarring.

All these reasons, if proved, should be important in burn therapy. But after the clinical use of pressure dressings at this hospital <sup>3</sup> and a critical survey of the literature, three reservations seemed indicated. The first was a practical point: Is there a true sparing action on loss of plasma or is the edema fluid merely displaced; how far can pressure be counted on to limit loss of plasma in the extensively burned patient? It was noted that in patients with burns of the extremities, the pressure of elastic bandages, even though applied well above the burn, often failed to check the appearance of edema in the unburned, unbandaged tissues. If both hands and wrists and the face were burned, for example (areas ideal for pressure bandaging), edema appeared in the upper part of the arms, at the base of the neck and over the chest.

Our failure to restrain the loss of plasma by pressure could have been due to an inadequate application of it, a fault which might be corrected by using the plaster dressing as recommended by Drinker. On the other hand, since the edema collected in the unburned tissues, proximal to the burn on the arms and over the upper part of the chest, perhaps it became disseminated because the lymphatic trunks draining the wound were overloaded, a factor which a plaster dressing might improve but not altogether correct. It should also be pointed out that Siler and Reid hesitated to draw a definite conclusion from their experiments aimed at testing the efficacy of pressure dressings in sparing loss of plasma.

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3. Cope, O., and Rhineland, F. W.: Symposium on the Management of the Cocoanut Grove Burns at the Massachusetts General Hospital: The Problem of Burn Shock Complicated by Pulmonary Damage, *Ann. Surg.* **117**:915, 1943.

The second reservation had regard to the rationale: Is the local collection of edema so deleterious to wound healing? It has been repeatedly observed at this hospital that the swelling of a burn wound may disappear almost as rapidly as it came and that fibrosis, or scarring, is by no means a constant sequel of preexisting edema. Bleb fluid from a partial thickness burn often fails to coagulate, and whether it does or not, it is resorbed in less than twelve days if the roof of the bleb is intact (and the wound uninfected). These findings would not suggest widespread coagulation of protein in the wound spaces in the absence of infection. They would also not suggest that distention of itself tears tissue.

The presence of infection, of course, might increase the coagulation *in situ* of the proteins which have exuded from the blood; but is coagulation so deleterious? Glenn, Gilbert and Drinker<sup>1c</sup> offered experiments which they believed point to such unfavorable action. They compare the healing of the two feet of dogs burned equally. One foot of each dog was encased immediately after the injury in either a plaster mold or a light plaster bandage. The control foot was left uncovered. Healing proceeded much more rapidly, with less destruction of tissue and less final scarring, in the foot encased with plaster. The improved healing is unquestioned, but in the appraisal of the result they laid such emphasis on the absence of coagulated protein in the wound that they neglected to consider the mechanical protection offered by the plaster. The cast must have cut down, if not cut out, the repeated bacterial contamination which the uncovered foot received from the skin elsewhere, the tongue and the cage.<sup>4</sup> If the dog used the foot, the cast should have distributed the pressure and protected the foot from the trauma of licking.

The third reservation is the possible harm which might accrue from improper application of a pressure or plaster bandage, a warning stressed by Glenn, Gilbert and Drinker.<sup>1c</sup> If the bandage does not include the most distal portion of an extremity, even though unburned, gangrene may result. Because of the haste which may necessarily accompany care of disaster casualties and the length of time needed to apply an effective restrictive dressing, particularly plaster, the virtues of such a dressing must outweigh this danger before such therapy can be recommended.

We agree with Levenson and Lund<sup>1d</sup> that the reports on the clinical use of plaster bandages, and particularly those of Glenn, Gilbert and

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4. The skin of dogs is heavily contaminated with fecal organisms, including the clostridia (Pope, A.; Zamecnik, P. C.; Aub, J. C.; Brues, A. M.; Dubos, R. J.; Nathanson, I. T., and Nutt, A. L.: *The Toxic Factors in Experimental Traumatic Shock: VI. The Toxic Influence of the Bacterial Flora, Particularly Clostridium Welchii*, in *Exudates of Ischemic Muscle*, J. Clin. Investigation **24**:856, 1945. Langohr, J. L.; Owen, C. R., and Cope, O.; Unpublished data).

Drinker<sup>1c</sup> on dogs, were so interesting that a more extended survey of their usefulness should be made. Since some of the supposed advantages and our own reservations are not susceptible to controlled testing on chance burns in the human being, resort was made to experiments on dogs, following the lead of Glenn, Gilbert and Drinker. Attention has been focused on the arterial and lymphatic circulation and their influence on the state of the wound. The observations bear only indirectly on the nutrition of the wound, for direct methods of sufficient accuracy have not been developed to compare the oxygen tension, for example, of the wound treated with a cast with that of the untreated wound.

#### EXPERIMENTS

The experimental animals were dogs of 18 to 20 Kg. They were anesthetized with pentobarbital sodium intravenously except in 2 cases in which sodium barbital was employed. The hair of the hindlegs was clipped closely. The method of burning was to plunge both hindfeet, to just below the ankle joint, for fifteen seconds into hot water at either 100 or 90 C. Immediately after burning, a thin skin-tight plaster bandage was applied to one foot, evenly without pressure, extending about 2 inches (5 cm.) above the burned area. The other foot was not enclosed in a cast and in the last experiments was covered with a dressing of loose petrolatum gauze. The surgical procedures, described under the separate headings, were performed with aseptic precautions, and the operative wounds were closed as much as the cannulas permitted. The collection of lymph samples from the cannula was not carried out aseptically, and the citrate solution used in the blood pressure determinations was not sterile.

In all, 33 dogs were used. In some experiments one type of observation was made, but in most data on various aspects were obtained.

1. *Lymph Flow*.—In experiments on 10 dogs the lymphatic vessels of the hindfeet just above the ankle were cannulated in routine manner. Lymph was collected for analysis over periods before burn and after burn. After the feet had been burned, one foot was enclosed in a cast and the other was not.

The results are shown in table 1. The initial increase in rate of lymph flow after the burn was more rapid in the foot with a cast. The rate rose, however, to a higher level in the foot without a cast, which confirmed the findings of Drinker<sup>1c</sup> with burns at 100 C. The same was true whether the burn was at 90 C. or at 100 C. and whether the feet were dependent or horizontal after the burn. The findings were consistent with one exception.

With the feet dependent, the 100 C. burn tended to produce a faster subsequent decrease of lymph flow in the foot with a cast (two of three

experiments), as Drinker<sup>1c</sup> observed with burns at this temperature. The 90 C. burn, on the other hand, led to a more rapid decrease in the foot without a cast (three of four experiments). With the feet horizontal and the burn at 90 C. (three experiments), the rate of subsequent fall of lymph flow averaged the same. Over the whole series of experiments there was thus no constant difference between the feet with a cast and those without a cast as far as the rate of subsequent fall of lymph production, after the initial rise following the burn, was concerned.

The effect of an intravenous infusion of isotonic sodium chloride solution was studied in 5 dogs. There was an almost immediate effect of increasing lymph flow. No difference was observed between legs treated with a cast and untreated legs as regards the amount and the rapidity of increased flow.

TABLE 1.—*Relative Rate of Lymph Flow From Feet With and Without Casts After Burning for Fifteen Seconds*

	No. of Dogs	Period of Increasing Flow						Subsequent Period of Decreasing Flow, Sharper Fall		
		Sharper Rise			Higher Peak Reached					
		Foot With Cast	Foot Without Cast	Same, Both Feet	Foot With Cast	Foot Without Cast	Same, Both Feet	Foot With Cast	Foot Without Cast	Same, Both Feet
Burn at 100 C.; dogs on back; legs dependent....	3	3	..	..	..	3	..	2	..	1
Burn at 90 C.; dogs on abdomen; legs dependent	4	4	..	..	..	4	..	..	3	1
Burn at 90 C.; dogs on abdomen; legs horizontal.	3	2	..	1	..	3	..	1	1	1

2. *Lymph Protein Concentration.*—In the 4 dogs burned at 100 C. and in 5 of the 6 dogs burned at 90 C. in which the lymph protein concentration was measured it was consistently slightly higher in the foot with a cast than in the foot without one for the period of the experiment following the burn (chart 1). In the sixth dog burned at 90 C. the protein concentration was lower in the foot with a cast after the first forty-five minutes following the burn. In this animal the peak of lymph flow reached in the other foot was only slightly above that in the foot with a cast, less so than in the other experiments; lymph flow ceased in the sixth hour. It is believed that the cannulation of lymphatic ducts was a poor mechanical preparation, and the data on lymph are therefore to be discounted. In keeping with the difference in protein concentration of the two lymphs, there was observed a difference in chloride concentration; it was lower in the lymph with the higher protein concentration. These observations cover a period up to eleven and a half hours after burn.

The effect of an intravenous infusion of isotonic sodium chloride solution on lymph protein concentration was studied in 4 of the animals (chart 1). The protein concentration was diminished in all burned feet except one not treated with a cast. In three of the experiments the fall in concentration was greater in the feet enclosed in a cast and in two of these the concentration in the feet so treated fell below that in

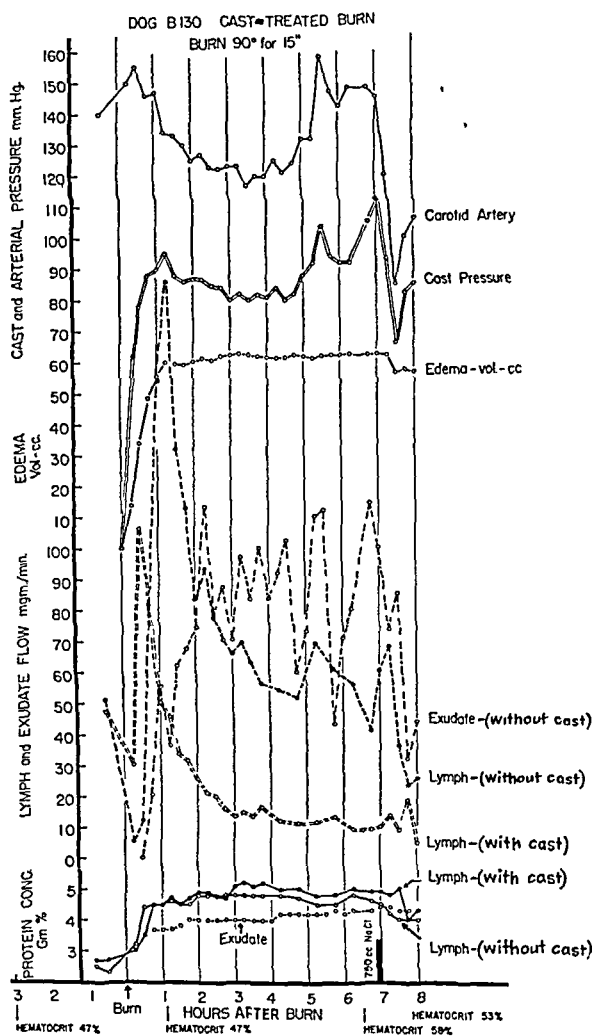


Chart 1.—Effect of restrictive plaster bandage on the lymph and exudate flow and protein concentration, edema formation and tissue and arterial pressure following burn of a hindfoot of a dog at 90 C. for fifteen seconds.

the feet without a cast. The maximal drop was noted at one to one and a half hours after the sodium chloride solution had been given.

3. *Venous Pressure.*—Venous pressures were compared after a burn of the hindfeet for fifteen seconds at 100 C. Determination of the venous pressure was carried out by inserting a large bore needle directly

into the main vein on the lateral aspect of the ankle. The needle was connected with a bromoform manometer, care being taken to eliminate the effect of gravity. Three of the experiments were considered satisfactory technically. In two of them the venous pressure showed a slight drop after the burn, but there was no significant difference between the legs with a cast and those without a cast. In 1 animal there was a slight rise after the burn and then a drop in both legs. The pressure in the leg without a cast stayed somewhat higher, the difference in height ranging between 0.5 and 1.0 cm. of bromoform.

4. *Arteriovenous Oxygen Differences.*—Preliminary experiments indicated that after a burn there was a large discrepancy between the venous oxygen content of blood taken from the femoral vein and that of blood from a vein in the lower part of the leg just above the burned area. The arteriovenous oxygen difference became extremely low when

TABLE 2.—*Arteriovenous Oxygen Differences (Values in Volumes Per Cent) in Blood Taken from the Femoral Artery and the Ankle Vein*

Dog No.		Before Burn	After Burn			
			1 Hour	3 Hours	6 Hours	10 Hours
B94	Foot with cast.....	0.8	0.0	0.1	1.5	0.5
	Foot without cast.....	0.0	0.0	0.1	0.2	1.2
	Control forefoot .....	2.2	0.4	0.3	2.6	2.4
B96	Foot with cast.....	3.6	0.0	0.1	0.2	1.1
	Foot without cast.....	3.8	0.2	0.1	0.2	1.1
	Control forefoot .....	3.6	0.9	0.8	0.9	2.7
B98	Foot with cast.....	2.9	1.3	2.1	1.5	2.8
	Foot without cast.....	2.8	0.6	0.8	0.9	2.7
	Control forefoot .....	1.0	0.9	...	1.2	2.7

the venous blood was taken from just above the site of the burn. Seven experiments were therefore carried out using a burn of 100 C. for fifteen seconds, venous blood being taken at the ankle and the arterial blood at the groin. In three the arteriovenous oxygen difference reached the lowest level in the leg without a cast, while in four it reached it in the leg with a cast. The difference between the values for the two legs was not significant, however, as is shown in table 2, which summarizes the data of the last three experiments performed in this series.

5. *Blood Flow.*—Measurement of the rate of blood flow through the arteries of the burned hindfeet, one in a cast and the other not, was made by means of flowmeters. The dogs were heparinized. The burns were for fifteen seconds at 90 C.

The flowmeters were of the constriction type with two verticle side arms, one proximal and one distal to the constriction, connected with each other by a U tube.<sup>5</sup> As the blood flowed through the con-

5. Drs. Gordon K. Moe and Dr. Friedrich W. Klemperer aided us in the construction and use of the flowmeters.

striction, the differential in height of the blood columns in the proximal and distal limbs of the U tube gave a measure of the pressure gradient on the two sides of the constriction. The flowmeters, which were made of glass tubing, were calibrated by running through them the dog's heparinized blood at known rates of flow. A table for each flowmeter was constructed from which the experimentally observed rates of flow were extrapolated. The primary aim of the experiment was to compare the changes in flow in the legs with a cast and those without a cast rather than to measure absolute flow in either. In application, the artery under observation was divided. Each end of the flowmeter was connected by a short piece of rubber tubing to a glass cannula inserted in the proximal and distal limbs of the artery. The top air-containing portions of the U tube of the flowmeter were connected by a Y tube to a mercury manometer in order to give a record of the blood pressure in the same artery in which flow was being recorded. Further details of the flowmeter method, including an illustration, are given in a subsequent paper.

In the first four experiments simultaneous recordings from the two femoral arteries were made. Each foot below the ankle was burned and a cast applied to one foot. An immediate rise occurred in the flow in each leg and then a gradual fall for the eight hours of the experiment. When a composite graph was made of the flows from the two legs in each of these four experiments, no significant differences between them were observed.

In order to evaluate more closely the blood flow through the burned portion of the legs alone, flowmeters were inserted into each anterior tibial artery, just above the ankle, in 3 animals. After the flowmeter had been inserted, the other main artery to the foot was ligated. In two experiments the flow for the first eight hours after burn was observed. In 1 case the flow in the two legs rose rapidly to essentially the same height and then showed the same subsequent slow fall. The maximum flow for the two legs was 45 to 50 cc. per minute at ten minutes after burn whereas the preburn rate had been 10 to 15 cc. per minute. In the other case the flows started at similar preburn levels. The first post-burn readings, made at one half hour, showed that the flow in the leg with a cast was at its maximum of 33 cc. per minute. The flow in the leg without a cast did not reach its maximum, a slightly less high level, until three hours later.

In the third dog with flowmeters in the anterior tibial arteries, the rate of flow for the second eight hours after burn was studied. The dog was burned, and the cast was applied immediately to one leg and loose petrolatum gauze to the other. The animal was kept under light anesthesia with pentobarbital sodium given intraperitoneally during the



first eight hours after burning, and the flowmeters were then inserted.<sup>6</sup> No significant differences were observed between the leg with a cast and the other leg. The flow in each leg continued to fall off during the period of observation from an average of 15 to 25 cc. per minute down to an average of 4 to 8 cc. per minute at sixteen hours after the burn.

6. *Tissue Pressure Beneath the Cast.*—The pressure which existed between the surface of a foot which had been burned and the inside wall of a cast surrounding this foot was measured by inserting a thin-walled rubber bulb under the cast at the time the latter was applied immediately after the burn. The rubber bulb was filled with water and connected with a mercury manometer which recorded on a smoked drum. An adjustable pressure bottle was attached to the recording system in such a manner that the volume of fluid within the rubber bulb under the cast could be kept constant at all times when a pressure reading was being recorded. Adjustment of the fluid volume within the rubber bulb was made at frequent intervals, and a tracing of the cast pressure was recorded simultaneously with a tracing of the carotid blood pressure on the same drum (chart 1).

The cast pressure was recorded in seven of the experiments in which the hindfeet were burned for fifteen seconds at 90 C. and in which the lymphatic vessels of the ankle had been cannulated. The end pressure in the lymphatic vessels themselves was not recorded. The lymph was allowed to flow freely. The lymph flow and the lymph protein concentration have been recorded in the previous sections. In six of the experiments the mean carotid arterial blood pressure was recorded simultaneously.

The cast pressure rose rapidly after the burn (chart 1). It reached its maximum in one to one and one-half hours. After having reached the maximum it varied closely with the blood pressure and in the various experiments ranged from approximately one half to two thirds of the mean arterial pressure.

Various factors influenced the relationship between cast pressure and blood pressure. In order to demonstrate these, two graphs were constructed for each of the 6 animals in this series, one of which is reproduced (chart 2). In graph A (the lower of the two graphs) the difference between mean arterial blood pressure and cast pressure is plotted as ordinates against the time after burn as abscissas. As the cast pressure approached its constant relationship with the blood pressure, the curve flattened out. High points on this curve, then represent

6. Up to the time of the insertion of the cannulas the dog had been placed on its side. In order to insert the flowmeters, the dog was placed on its back, the position used in the previous experiments. Respirations, however, faltered, and the animal became cyanotic. It was returned to its side, with slow improvement, and the operation and experiment were completed in this position.

greater than average difference between blood pressure and cast pressure, and low points represent less than average difference. Each point on the graph has been given a number corresponding with the numerical sequence of half-hour periods following the burn.

In graph *B* (the upper of the pair of graphs in chart 2), the mean arterial blood pressures at each half-hour reading are plotted as ordinates against the corresponding cast pressures as abscissas. This gives a series of points which are designated with the same numerals, corresponding to half-hour periods after

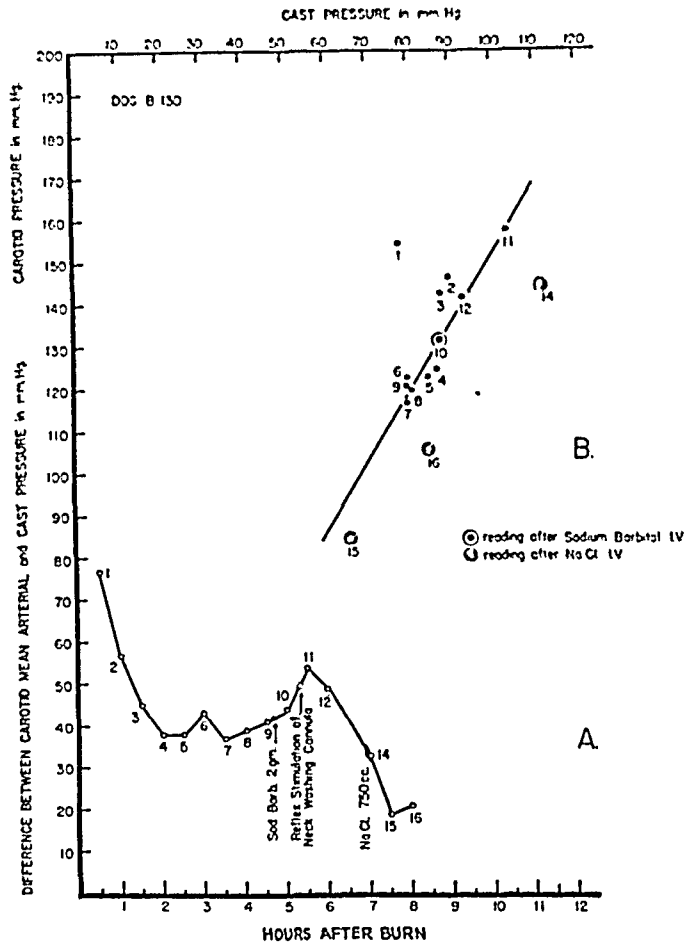


Chart 2.—Relationship of cast pressure to arterial blood pressure.

burn, that are employed in graph *A*. Graph *B* for each animal indicates that at a higher systolic blood pressure there is normally a greater difference between cast pressure and blood pressure than there is at a lower blood pressure. This fact accounts for some of the points in graph *A* of the various experiments which were situated unusually high above the horizontal mean of the graph.

The type of graph designated as *B* serves to demonstrate variations from the normal range in the cast pressure versus blood pressure relationship when a large amount of isotonic sodium chloride solution was rapidly injected intravenously. That such an injection produced a narrowing of the cast pressure—

blood pressure difference had been suggested but not proved by graph *A*. The method of plotting employed in graph *B* eliminates the variable introduced by different levels of blood pressure and demonstrates that this narrowing was a true effect of the sodium chloride solution irrespective of changes in blood pressure. Thus in graph *B* for each animal the points following the intravenous injection of isotonic sodium chloride solution lie farthest to the right of and below the mean of all the points recorded.

Another extrinsic factor which might have altered the cast pressure-blood pressure relationship was the intravenous injection of pentobarbital sodium to supplement the anesthesia. Two successive doses of this drug within half an hour led to a relative increase in the cast pressure with respect to the blood pressure in one experiment. A single large dose produced the same effect in another. When smaller doses of supplementary barbiturates were administered to these 2 dogs, and to other dogs, there was no demonstrable effect on the cast pressure-blood pressure relationship.

All the abnormally low points on graph *A* for the 6 dogs are explained by the administration of either isotonic sodium chloride solution or a large dose of pentobarbital sodium. All the abnormally high points in graph *A* of the six experiments covering up to nine and a half hours after burn are accounted for by the normal lag in cast pressure which takes place when the blood pressure goes to high levels. For example, the high point 11 on graph *A* of dog B130 (chart 2) followed reflex elevation of the blood pressure from manipulation of the neck when the carotid cannula was washed after clotting. Graph *B* demonstrated that point 11 lay near the mean.

7. *Edema in Legs Not Treated with a Cast.*—In 5 of the dogs in which tissue pressure beneath the cast was studied, the swelling of the simultaneously burned opposite hindleg, not enclosed in a cast, was recorded in a plethysmograph. In four experiments the leg was suspended vertically, and in the fifth experiment it was held horizontally. Oil was used in the plethysmograph so that the exudate from the burned foot could be recovered and measured separately. The oil which was displaced as the foot swelled was collected in a buret from which was read in cubic centimeters the amount and rate of edema formation.

In all experiments a rapid increase in edema was observed for the first one and a quarter to two hours after the burn (chart 1). In three of the experiments with the legs dependent, the maximum level was reached within the first two hours, which was maintained until the infusion of isotonic sodium chloride solution (chart 1). In the fourth instance, after the maximum initial rise a further gradual rise continued until the end of the experiment. In the experiment with the legs horizontal, a gradual rise continued until three and a half hours after burn, when it leveled off.

The edema formation corresponded with the rise in cast pressure on the opposite foot, but with the expected lag. As would also be anticipated, the effects on edema of blood pressure variation and adminis-

tration of sodium chloride solution were much less than the corresponding effects on the cast pressure.

*S. Rate of Exudate Formation in Legs Not Treated with a Cast.*—The exudate collecting under the oil at the bottom of the plethysmograph in four of the experiments described in the previous section was drawn off periodically by means of a separatory funnel, and its volume was measured. The exact moment when exudate formation began could not be determined. The moment when the first drop of exudate was large enough to fall to the bottom of the plethysmograph varied in the four experiments from between three-quarters of an hour and one and one-half hours after burn. Drops of exudate appeared in all areas of the burned skin and not merely from between the toes where actual blebs formed. The maximum rate of exudate formation was observed in the plethysmograph at from one and three-quarters to two and one-quarter hours after burn in the 3 dogs whose legs were in the dependent position (chart 1). In the experiment with the leg horizontal, the maximum exudate formation occurred at three hours after burn. Variations in rate of exudate formation with changes in blood pressure were observed in all four experiments and were of the same order.

*9. Exudate Protein.*—The protein concentration of the exudate fluid in each sample was measured in the four experiments in which exudate was recovered. In all instances the amount of exudate protein was lower than the protein concentration of the lymph collected from the lymphatic trunk of the same leg (chart 1).

#### COMMENT

The experimental explorations into the disordered physiologic changes in the burn wound supported by a rigid plaster of paris dressing recorded in this paper do not provide the unequivocal evidence needed to guide us in the use of pressure dressings in the treatment of burns. Changes encountered immediately after the burn which are apparently in favor of pressure dressings are supplanted with the passage of time. The other factors believed to favor these dressings, such as the decrease in proteins coagulated in situ and localization of infection, are still experimentally unproved.

The most emphasized benefit to be derived from pressure dressings is the sparing of the loss of plasma into the burn wound. However, Siler and Reid,<sup>1b</sup> after their experimental investigation which tended to show such a sparing, wisely pointed out in the discussion that the data they obtained were probably within the experimental error of the method used. Of like negative value are our own findings. At first sight the observation that the lymph flow from a burn wound is reduced by a rigid plaster wall applied immediately after injury should indicate

a diminished loss of plasma. As the experiment is followed, however, it becomes clear that the increased flow after burning is not sufficiently reduced by the cast for the lymphatic vessels to be able to carry it. Unable to return to the blood stream all the fluid flowing through the damaged capillaries, the lymph piles up as edema in the interstitial spaces proximal to the cast. With the passage of time this edema may slowly reach the volume it would have been had the restricting dressing not been applied.<sup>7</sup> Though in the first hours the volume of plasma lost may be reduced, it appears that eventually it may be the same as in the wound not treated with a cast. More quantitative evidence is, however, needed on this point.

The observations that the arterial blood flow to a burn wound is not reduced and that the arteriovenous oxygen difference is not altered by the plaster dressing suggest that no harm accrues to the wound's circulation and nutritional environment from the restricting pressure. It is possible that the benefit which clinically appears to accrue from the use of the restrictive dressings comes from the immobilization of the wound provided by the dressing. Motion of the burn wound increases lymphatic flow and displaces edema proximally in the interstitial spaces. These both have the effect of lowering the tissue pressure in the wound, which permits augmented seepage out of the capillaries. Because of these effects of motion and because the loss of plasma is retarded, restrictive, immobilizing dressings are presumably indicated in the care of burn wounds. They must not be used, however, with the idea that the need for plasma therapy in burn shock will be materially reduced. And whether the benefit from their use outweighs the danger of gangrene from improper application, particularly that of the plaster dressing, will depend on the intelligence with which such dressings are used.

#### SUMMARY

The effect of a restrictive plaster bandage on the disordered physiologic changes in the burn wound has been explored experimentally in burned feet of dogs. Although the increased flow of lymph from the burn is reduced toward normal, it is not sufficiently reduced to permit

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7. Our findings are not in agreement with the point of view of Glenn, Gilbert and Drinker<sup>10</sup> that "the enclosure of the burned part in a plaster of Paris dressing prevents abnormal leakage from the injured capillaries." The volume of lymph flowing from a burn wound restricted by plaster is not as great as from a wound allowed to swell, but it is far greater than normal, indicating an increased leakage of plasma fluid into the wound through the damaged capillary membrane. The inflow of arterial blood does not meet a truly rigid wall as conceived of by Glenn and others; the continued outflow of venous blood and lymph provides elasticity. The pressure within the cast does not reach mean arterial pressure.

the lymphatic vessels to carry the load, and edema piles up in the interstitial spaces of the leg proximal to the plaster bandage.

Loss of plasma volume is thus retarded but not eliminated and presumably not reduced. The concentration of the protein in the lymph flowing from the bandaged foot is slightly higher than in that from the foot allowed to swell, which indicates a greater resorption of water into the venous blood.

Venous pressures, arteriovenous oxygen differences and arterial blood flow were not altered by the plaster bandage.

Tissue pressure, measured as the pressure between skin and plaster bandage, approached but never reached mean arterial blood pressure. Arterial blood therefore does not flow against a rigid wall, the outflow of venous blood and lymph providing some elasticity.

The protein concentration of exudate fluid seeping out onto the surface of the burned skin is slightly lower than that of the lymph flowing from the same wound. This indicates either that water is resorbed from lymph, lymph being more concentrated than extracellular tissue fluid, or that part of the protein of the tissue fluid is strained as the fluid seeps through the skin. If the latter were true, the concentration of protein in the bleb fluid of a burn in the human being might be lower than that of the subcutaneous edema fluid.

The possible benefits and limitations of restrictive dressings are discussed.

# MORTALITY AND MORBIDITY IN SURGERY OF THE BILIARY TRACT

A Comparison of Two Consecutive Ten Year Periods

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ADVANCEMENTS made in the last few years in preoperative and postoperative care, such as better intravenous administration of fluids, amino acid and protein hydrolysates, antibiotic drugs like penicillin and the sulfonamide compounds, more available blood transfusions, vitamin K and better anesthetic procedures, should all reflect on the mortality of surgery of the biliary tract. A report in 1946 by Sanders<sup>1</sup> suggested that the mortality rate had not been reduced appreciably, whereas Orr's<sup>2</sup> recently reported statistics showed a definite improvement (table 1).

In this series the mortality has been markedly decreased in the last ten years as compared with the preceding ten year period (table 2). The decrease was from 8.3 per cent in the years 1927 to 1937 to 2.8 per cent in the years 1937 to 1947. The improvement is noted particularly in the cases of acute cholecystitis and in the marked decrease in deaths due to infection and peritonitis. The lowered mortality in this group is of interest in view of the controversy regarding immediate surgical treatment of acute cholecystitis versus delayed treatment. In spite of the fact that in the last ten year period there was a greater delay from the time of hospitalization to the time of operation, there has been a sharp decline in the mortality (table 3). Perhaps the lowered mortality credited by some authors to earlier operation may be due to the use of the antibiotics and to improved preoperative and postoperative care.

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From the Surgery I Service of St. Luke's Hospital.

Presented before the Chicago Surgical Society May 7, 1948.

1. Sanders, J. T.: Biliary Tract Surgery: An Inquiry into the Reason for the Thirty-Three Deaths in Four Hundred and Fifty-Three Operations, *South. M. J.* **39**:961 (Dec.) 1946.

2. Orr, T. G.: A Study of the Mortality Rate in a Series of Cholecystectomies, *Am. J. Digest. Dis.* **14**:89 (March) 1947.

The incidence of perforations of the gallbladder in this series was 18.1 per cent in the first ten year period, with a mortality of 33 per cent, and 26.6 per cent in the second ten years, with no deaths. Cowley and Harkins<sup>3</sup> in 1943 reported an incidence of perforation of

TABLE 1.—Mortality in Surgery of the Biliary Tract

Author	Year	Number of Cases	Mor- tality, %
Heuer <sup>4</sup> .....	1931	36,623	6.6
Ellason and Erb, Ann. Surg. 101:460 (Jan.) 1935..	1935	537	8.0
Heyd <sup>5</sup> .....	1910	557	7.7
Sanders <sup>1</sup> .....	1916	453	7.2
Orr <sup>2</sup> .....	1916	558	2.8
Diffenbaugh and McArthur.....	1927 to 1937	408	8.3
	1937 to 1947	417	2.9

TABLE 2.—Mortality Statistics

Condition for Which Operation Was Performed	Years	Cases	Deaths	%
Total mortality .....	1927 to 1937	408	34	8.3
	1937 to 1947	417	12	2.8
Acute cholecystitis .....	1927 to 1937	33	10	30.3
	1937 to 1947	30	1	3.3
Chronic cholecystitis with involvement of the common duct .....	1927 to 1937	85	16	18.8
	1937 to 1947	62	7	11.2
Chronic uncomplicated cholecystitis.....	1927 to 1937	270	4	1.4
	1937 to 1947	295	0	0.0
Malignant processes .....	1927 to 1937	9	3	33.3
	1937 to 1947	11	4	36.3
Secondary procedures on the common duct..	1927 to 1937	11	1	9.0
	1937 to 1947	19	0	0.0
1927 to 1937	70.2% of the deaths were in patients over 50 years of age.			
1937 to 1947	61.5% of the deaths were in patients over 50 years of age.			

TABLE 3.—Acute Cholecystitis

	1927 to 1937	1937 to 1947
Total cases .....	33	30
Males .....	31%	45.1%
Females .....	69%	54.9%
Perforations .....	18.1%	20.6%
Average time from onset of symptoms to hospitalization, days	3.2	2.2
Delay from time of hospitalization to operation, days.....	3.9	6.6
Complications involving the common duct.....	15.1%	6.6%
Stones .....	78.7%	90.3%
Mortality * .....	30.3%	3.3%

\* Eighty-one and one-tenth per cent of the deaths were due to peritonitis or infection.

13 per cent in 2,261 cases of acute cholecystitis, with a mortality of 20.8 per cent in the cases of perforation, and Heuer<sup>4</sup> in 1934 reported an incidence of 20 per cent, with a mortality of 45 per cent.

3. Cowley, L. L., and Harkins, H. N.: Perforations of the Gall Bladder, Surg., Gynec. & Obst. 77:661 (Dec.) 1943.  
4. Heuer, G.: Factors Leading to Death in Operations upon the Gall Bladder and Bile Ducts, Ann. Surg. 99:881 (June) 1934.



The mortality in cases involving the common duct decreased from 18.8 to 11.2 per cent. There is an inevitable increase in mortality in these cases, approximately three times that for cases of uncomplicated chronic cholecystitis. The common duct was explored in 25.9 per cent of cases in the 1927-1937 series and in 17.3 per cent of cases in the 1937-1947 series and stones were found in 28.2 and 36.6 per cent respectively (table 4). It is noted that in approximately one fourth of the cases in which the common duct was explored there was no jaundice or history of jaundice, yet stones were found in a considerable percentage (15.8 and 35.2 per cent). In the cases in which there was exploration of the common duct without drainage it was carried out through the stump of the cystic duct. The cystic duct was then ligated. In all cases in which the common duct was incised for exploration drainage was instituted. T tubes were used more fre-

TABLE 4.—*Complications Involving the Common Duct*

	1927 to 1937	1937 to 1947
Primary exploration of the common duct.....	25.9%	17.3%
Stones.....	28.2%	36.6%
Jaundice.....	77.6%	71.8%
Stones.....	31.8%	38%
No jaundice or history of jaundice.....	22.3%	23.9%
Stones.....	15.8%	35.2%
Drainage of the common duct.....	83.5%	74.6%
T tubes.....	2 cases	34 cases
McArthur double catheter.....	48 cases	15 cases
Single catheter.....	21 cases	4 cases
Secondary exploration of the common duct.....	11 cases	19 cases
Jaundice.....	62.5%	83.3%
Stones.....	54.5%	57.8%

quently in the last ten years than in the preceding ten. Before good solutions were available for intravenous administration a small catheter was frequently passed through the ampulla into the duodenum for the instillation of fluids and bile and a catheter passed up the duct for drainage. This method was used frequently in the first ten year period.

The mortality for secondary procedures on the common duct was 9 per cent in the first ten year period; in the last ten years there were no deaths. Heyd<sup>5</sup> has stated that whereas the mortality in cases involving the common duct is about 11.3 per cent when the exploration is performed at the time of the original cholecystectomy, in secondary choledochotomy the mortality is 350 per cent greater, i. e., the rate is 38.6 per cent.

Table 5 lists both minor and fatal complications occurring in this series. Pulmonary, vascular and hepatic complications were as frequent

5. Heyd, C. G.: Factors in the Mortality in 4,000 Operations upon the External Biliary System, *Ann. Surg.* **111**:820 (May) 1940.

in the last ten years as in the first ten, but less fatalities resulted. Hemorrhage and infection as complications were markedly decreased in the last ten years as compared to the previous ten year period Chart 1 shows this graphically.

The causes of death in this series were obtained from clinical records and from the findings at postmortem examination (1927 to 1937, autopsy in 53 per cent of cases; 1937 to 1947, autopsy in 75 per cent). Tables 6, 7 and 8 list the causes of death in the cases of acute cholecystitis, chronic cholecystitis and involvement of the common duct.

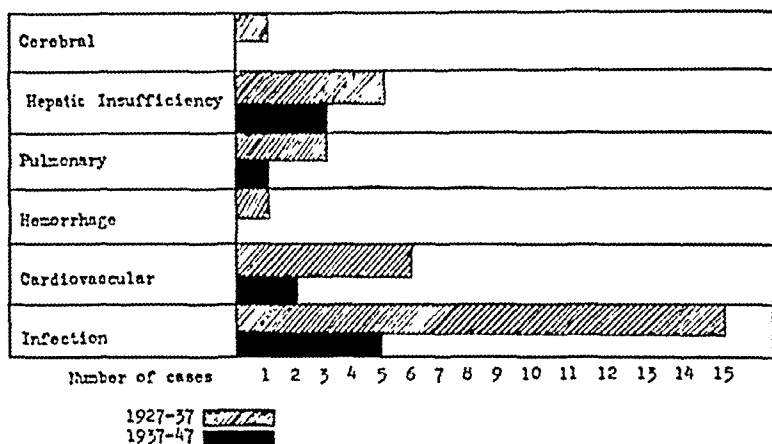


Fig. 1.—Causes of death.

TABLE 5.—Statistics on Morbidity and Mortality

	1927 to 1937	1937 to 1947
Pulmonary complications.....	7	10
Pneumonia.....	4	2
Pleurisy.....	1	3
Atelectasis.....	..	5
Cardiovascular complications.....	8	6
Coronary occlusion.....	2	1
Congestive failure.....	4	3
Pulmonary embolus.....	2	2
Hepatic insufficiency.....	2	6
Cholemia.....	2	1
Hepatorenal syndrome.....	..	5
Hemorrhage.....	8	1
Evisceration.....	..	1
Infection.....	29	9
Wound infection.....	17	3
Subdiaphragmatic abscess.....	..	1
Thrombophlebitis.....	..	2
Cholangitis.....	7	2
Peritonitis.....	5	1
Bile collections.....	1	1
Acute pancreatitis.....	..	3
Functional		
Postoperative colic.....	6	5
Distention.....	5	3

TABLE 6.—*Causes of Death in Cases of Acute Cholecystitis*

1927 to 1937		1937 to 1947	
Peritonitis.....	5	Pneumonia.....	1
Sepsis.....	3		—
Pneumonia.....	1		1
Acute suppurative cholangitis.....	1		
	—		
	10		

TABLE 7.—*Causes of Death in Cases of Chronic Cholecystitis*

1927 to 1937		1937 to 1947	
Peritonitis.....	2	No deaths	
Coronary occlusion.....	1		
Hepatic necrosis.....	1		
	—		
	4		

TABLE 8.—*Causes of Death in Cases Involving the Common Duct*

1927 to 1937		1937 to 1947	
Peritonitis.....	5	Peritonitis.....	1
Suppurative cholangitis.....	1	Acute pancreatitis.....	3
Sepsis.....	2	Hepatorenal syndrome.....	1
Bronchopneumonia.....	2	Coronary occlusion.....	1
Pulmonary embolism.....	1	Pulmonary embolism.....	1
Cerebral embolism.....	1		—
Cardiac failure.....	2		7
Coronary thrombosis.....	2		
Hemorrhage.....	1		
Cholemia.....	3		
	—		
	20		

TABLE 9.—*Causes of Death in Operations on the Gallbladder (Cole<sup>8</sup>)*

	Stanton <sup>6</sup> (from Litera- ture), %	Colp and Ginzberg <sup>7</sup> (Own Cases), %	Heuer <sup>4</sup>	
			1,000 Cases (Own), %	36,623 Cases (from Litera- ture), %
Peritonitis.....	15.4	16.5	37	33
Shock.....	5.0	...	..	..
Pneumonia.....	10.6	9.3	25	20
Pulmonary embolus.....	6.6	2.0	..	..
Cardiac failure.....	6.8	3.1	10	12
Renal failure.....	4.8	3.1	..	..
Operative hemorrhage.....	6.4	3.1	..	..
High temperature.....	4.0	...	..	..
Cholemia.....	4.4	...	..	..
Cholemia with hemorrhage.....	4.0	...	..	..
Hepatic insufficiency.....	3.8	...	..	4
Sepsis.....	3.2	3.1	..	..
Evisceration.....	0.2	3.1	..	..
Suppurative cholangitis.....	4.0	14.4	..	..
Pylephlebitis.....	...	8.2	..	..
Pancreatitis.....	...	5.2	..	2
Injury or stricture of the common duct	...	9.3	..	..
Gangrene or perforation.....	...	...	11	10
Miscellaneous.....	...	...	17	19

Infection and peritonitis were the most important causes of death in the first ten year period but were less a factor in the last ten years.

Stanton <sup>6</sup> in a review of 500 cases involving the biliary tract in which death followed operation and in which postmortem examination had been carried out, classified the causes of death as follows: infection and peritonitis, 38.4 per cent; hepatic insufficiency, 22 per cent; cardiovascular disease, 12.8 per cent; shock and hemorrhage, 11 per cent, and pneumonia, 10.6 per cent. These are approximately the percentages as reported by Colp and Ginzberg <sup>7</sup> and by Heuer <sup>4</sup> (table 9 from an article by Cole <sup>8</sup>).

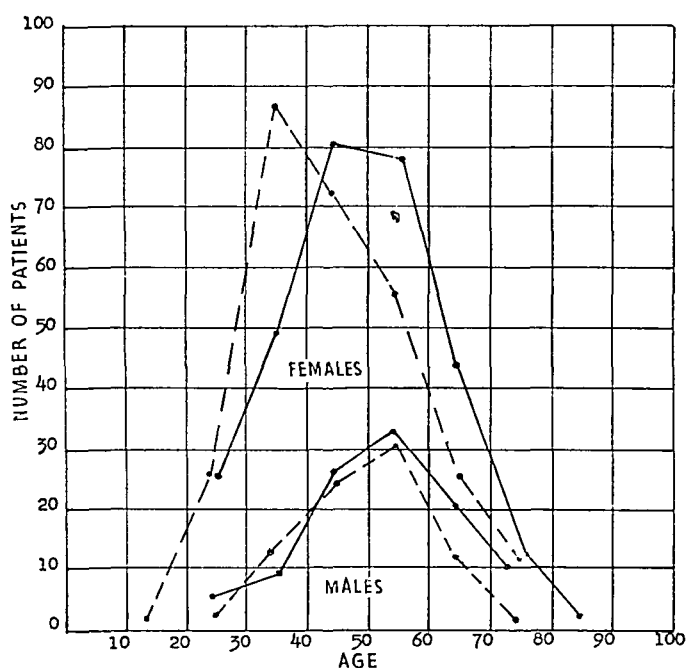


Fig. 2.—Age incidence of patients at the time of operation. Broken line is for the years 1927 to 1937 and solid line for the years 1937 to 1947.

Chart 2 is a graph of the peak age at the time of operation. The greatest number of men were between 50 and 60 years of age. This has remained the same throughout the two periods, but the age of the women has shifted from between 30 and 40 years to nearer 50 years. One would expect this to reflect adversely on the mortality statistics.

6. Stanton, E. M.: Immediate Causes of Death Following Operations Upon the Gall Bladder and Ducts, *Am. J. Surg.* 8:1026 (May) 1930.

7. Colp, R., and Ginzberg, L.: Mortality in Surgical Diseases of the Biliary Tract, *Ann. Surg.* 105:9 (Jan.) 1937.

8. Cole, W. H.: Factors in the Prognosis and Mortality of Gall Bladder Disease, *Internat. Abstr. Surg.* 69:40 (July) 1939.

In chart 3 it is shown that acute infection of the gallbladder, hemorrhage, jaundice and involvement of the common duct, age and sex are all factors influencing mortality. Seventy and one-fifth per cent of the deaths in the first ten year period were in patients 50 years of age or over and 61.5 per cent in the second ten years. Hemorrhage, although a complicating factor in the last ten years, was not a significant influence in any fatality in this period, whereas it was in the first ten years. Thirty per cent of the deaths in the first ten years involved patients with acute cholecystitis and 12.5 per cent of those in the second ten year period. Fifty-six and three-fifths per cent of the patients who died in the first ten years were jaundiced and 75 per cent of those in the last ten year period; 40 per cent in the first ten year period were men and 50 per cent in the last ten years, whereas men comprised only 23.6 per cent and 27.3 per cent of the total cases in this series.

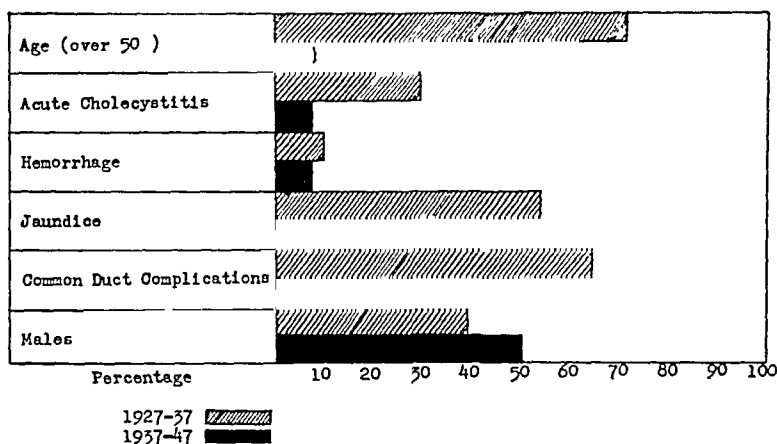


Fig. 3.—Factors contributing to mortality.

Cole,<sup>8</sup> in this regard, stated that whereas males were not as likely as females to have cholecytic disease, they were much more likely to have complications when it did develop.

#### SUMMARY

In this series the mortality in surgery of the biliary tract has been greatly reduced in the last ten years as compared with the preceding ten year period. This is noted particularly in the decrease in deaths due to infection and peritonitis.

The mortality of operation for uncomplicated chronic cholecystitis is lower than that of any other intra-abdominal procedure, but the rate rises rapidly when there are complications of the disease.

Age with its associated degenerative diseases, acute inflammation of the gallbladder or the ducts, hemorrhage, jaundice and complications involving the common duct contribute to the mortality.

# ABDOMINAL OPERATIONS ON PATIENTS WITH CHRONIC PARAPLEGIA

Report of Cases

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THE LARGE number of patients with chronic paraplegia inherited by the United States from World War II are posing problems for every specialty in medicine and surgery. Some of these, such as patients with medical, neurosurgical, urologic, orthopedic and sociologic problems, those with decubitus ulcers and those with the problem of rehabilitation, have been dealt with in a number of publications.<sup>1</sup> Little has been mentioned of the problem of abdominal surgery,<sup>2</sup> which, though it occurs less often, is nevertheless important in the over-all management of the cases.

Patients with severe neurologic defects and anesthesia below the level of injury, with their ubiquitous medical and urologic complications and bed sores, tax the diagnostic acumen and the judgment of the surgeon

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From the Surgical Service, Veterans Administration Medical Teaching Group, Kennedy Hospital.

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1. Freeman, W., and Heinburger, R. F.: The Surgical Relief of Spasticity in Paraplegic Patients: I. Anterior Rhizotomy, *J. Neurosurg.* **4**:435, 1947. Petroff, B. P.: War Wounds of Spinal Cord: The Paralyzed Patient; Urologic Aspects, *J. A. M. A.* **129**:154 (Sept. 8) 1945. Thompson, G. J.: Cord Bladder, Restoration of Function by Transurethral Operation, *U. S. Nav. M. Bull.* **45**:207, 1945. Munro, D.: The Rehabilitation of Patients Totally Paralyzed Below the Waist, With Special Reference to Making Them Ambulatory and Capable of Earning Their Own Living: III. Tidal Drainage, Cystometry and Bladder Training, *New England J. Med.* **236**:223, 1947. Munro, D.: Care of the Back Following Spinal Cord Injuries: A Consideration of Bed Sores, *New England J. Med.* **223**:391, 1940. Martin, J., and Davis, L.: Studies Upon Spinal Cord Injuries: I. The Development of Automatic Micturition, *Ann. Surg.* **126**:633, 1947. Conway, H.; Kraissl, C. J.; Clifford, R. H., III; Gelb, J.; Joseph, J. M., and Leveredge, L. L.: The Plastic Surgical Closure of Decubitus Ulcers in Patients with Paraplegia, *Surg., Gynec. & Obst.* **85**:321, 1947. Kostrubala, J. G., and Greely, P. W.: The Problem of Decubitus Ulcers in Paraplegics, *Plast. & Reconstruct. Surg.* **2**:403, 1947.

2. Hoen, T. I., and Cooper, I. S.: Acute Abdominal Emergencies in Paraplegics, *Am. J. Surg.* **75**:19, 1948.

who is called to see those among them who are suspected of having abdominal conditions. It is intended to discuss this phase of the paraplegic management and to present cases in which operation was performed by members of the surgical staff of the Kennedy Veterans Administration Hospital.

#### SYMPTOMS

Pain is a presenting symptom in the patients with acute abdominal conditions. The pain is usually poorly localized, dull and oppressing. Occasionally it may be sharp and recurrent. If the pain is sharp and knifelike with a radicular distribution, then the neurologic lesion must be ruled out as the cause of the pain. This is best done by consultation with the neurologist or the neurosurgeon. The next most common causes of abdominal pain in the paraplegic patients are urinary infection and calculi. Nausea and vomiting frequently accompany the pain in the urologic conditions. Because the patients practically always have cellular elements in the urine, urinalysis is usually of little help. Spasm and perforation of the bladder must be constantly borne in mind. Whenever there is the possibility of a urologic condition, consultation with the urologist is a must.

It is difficult to explain how these paraplegic patients perceive pain from the abdominal viscera. It seems that the abdominal viscera or at least their mesenteries are supplied with sensory nerve endings. The studies of Ray and Will indicate that in general the pain stimuli from the gastrointestinal tract are carried by the sympathetic fibers with the exception of the oral and distal colonic ends of the alimentary tract, which also have somatic pathways, and the bladder, which has parasympathetic as well as somatic pathways in addition to the sympathetic.<sup>3</sup> Conduction of painful sensation from the viscera to the spinal cord may be by way of the thoracic, splanchnic, hypogastric and pelvic nerves and thence over the posterior roots.<sup>4</sup> According to White, it is incorrect to consider the visceral sensory neurons as sympathetic nerve fibers, since they are mixed nerves containing a large preponderance of sympathetic motor fibers which belong to the posterior spinal root.<sup>5</sup> Although visceral sensation is conducted by the posterior root system similar to pain from the abdominal wall or the extremities, yet the pathways of reception of visceral sensory impulses and of somatic sensory impulses must be different, because many paraplegic patients with a physiologically complete division of the cord cannot perceive sensory somatic

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3. Ray, B. S., and Neill, C. L.: Abdominal Visceral Sensations in Man, *Ann. Surg.* **126**:633, 1947.

4. White, J. C., and Smithwick, R. H.: *The Autonomic Nervous System*, New York, The Macmillan Company, 1945. Ray and Neill.<sup>3</sup>

5. White, J. C.: *Sensory Innervation of the Abdominal Viscera Pain*, Baltimore, Williams & Wilkins Company, 1944.

stimuli below the dermatome level of cord transection but can perceive painful stimuli from the viscera whose sensory fibers are believed to enter posterior roots below the level of division.<sup>2</sup> It has been noted that visceral pain satisfactorily relieved by bilateral cordotomy often gradually returns and that visceral pain pathways may have accessory pathways by which they reach the sensorium.<sup>6</sup> It has been suggested that visceral pain impulses may pass cephalad for several segments in the sympathetic ganglionic chain before entering the cord.<sup>2</sup> This could explain how pain is perceived in some cases, but does not explain the pain in all cases. Hoen and Cooper cited a quadriplegic patient with transection of the cord at the sixth cervical root who had sharp stabbing pain in the epigastrium due to gastric ulcer, the presence of which was confirmed by roentgenograms.<sup>2</sup> In such an instance, even the explanation that escape from injury of accessory pathways in the cord, represented by relays of short neurons close to the spinal gray matter,<sup>7</sup> is not satisfactory. It may be that in certain instances painful impulses from the stomach may be transmitted via the vagus nerves,<sup>8</sup> although Alvarez, among others, stated that vagotomy does not interrupt pain pathways from any of the viscera.<sup>9</sup> Fortunately the paralysis is incomplete in some cases, and in these the perception of pain may be no problem.

Because of flaccidity or spasticity, abdominal rigidity may be absent or unrecognizable, but a slight sense of resistance has been noticed with underlying infection.

Tenderness is not common in these patients but has been elicited, and when present it is of significance. In a paraplegic patient with a ruptured bladder tenderness was elicited in the suprapubic region.<sup>2</sup>

Nausea and vomiting are usually present in cases of acute abdominal conditions but can be misleading because paraplegic patients become nauseated and vomit more commonly from various causes than non-paraplegic patients. Nausea and vomiting are common with the urinary infections and urinary calculi, which the majority of these patients have at one time or another. Likewise, anorexia is so common that it becomes of no diagnostic value, unless it is a noticeable change from the previous condition.

Elevation of temperature is common in the paraplegic patient. A sudden rise to 103 F. or over is usually indicative of urinary sepsis. Sudden rises to lower temperatures occur in patients with acute abdomi-

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6. Livingston, W. K.: *Pain Mechanisms*, New York, The Macmillan Company, 1944.

7. Karpus, J. P., and Kreidl, A. E.: Ein Beitrag zur Kenntnis der Schmerzleitung in Rückenmark, *Arch. f. d. ges. Physiol.* **158**:275, 1914.

8. Hoen and Cooper.<sup>2</sup> White and Smithwick.<sup>4</sup> Livingston.<sup>6</sup>

9. Alvarez, W. C.: Therapeutic "Information Please," *Gastroenterology*, J. A. M. A. **132**:970 (Dec. 21) 1946.



nal conditions and in those with phlebothrombosis. Elevation of the white blood cell count is of value only if a recent count has been made which could be used as a base line. A rapid pulse may give an important lead to a correct diagnosis of the acute abdominal condition.

Absence of intestinal sounds is only of value if it is known that they were present previously. Constipation and distention is so common in the otherwise "healthy" paraplegic patient as to be of no value in diagnosis. Likewise, air-filled, dilated intestinal loops are so frequent in ordinary patients with paraplegia that they are of no diagnostic value when seen on a roentgenogram of the abdomen. On the other hand, when fluid levels are seen, they have the usual significance. Demonstration of calculi in flat roentgenograms and in pyelograms in a case in which they were not previously present is of great help. After operative procedures, such as resection of the neck of the bladder, distention and ileus may be distressing to the uninitiated. Intestinal intubation with Wangenstein suction and enemas will frequently relieve the situation in a short time.

Fecal impaction should not act as a pitfall in diagnosis. Often the rectal examination, with removal of a hard bolus, will relieve all concerned, including the patient.

Jaundice has been more common in the paraplegic patients than in others. It is not known as yet whether this is due to the infectious hepatitis or to the transfusions of blood and plasma which most of them have received. Liver function studies, roentgenograms of the abdomen and cholecystograms may indicate whether biliary obstruction is the cause.

The diagnosis of acute trauma of the abdomen is made as in the normal person with the added handicap of the possibly absent tenderness, rigidity or localizing pain discussed previously. Referred pain may be of aid in diagnosis, as in the case of the ruptured spleen, presented later.

In addition to the acute abdominal conditions, there are others which require decisions on the part of the general surgeon. For example, the paraplegic patient with spasticity who has an inguinal hernia should have it repaired to avoid strangulation, although this complication has not been observed in the cases presented here.

Recognition of complications of abdominal surgery, such as subphrenic abscess, peritonitis and phlebothrombosis, requires a greater awareness on the part of the surgeon than is generally the case. In dealing with paraplegic patients he must "look for trouble," for reasons already discussed.

#### REPORT OF CASES

CASE 1.—F. K., a 29 year old white man, was injured on Oct. 11, 1946, which resulted in a fracture of the twelfth thoracic vertebra, with anterior displacement

of the eleventh and twelfth thoracic vertebrae, and paralysis, atrophy and complete anesthesia and analgesia below the eleventh thoracic dermatome anteriorly and posteriorly. Deep pressure was present down to the groin areas bilaterally. Vibration sense was present over the iliac spine. The upper abdominal reflexes only were present. He had paralysis, with incontinence of the bladder, for which a suprapubic cystotomy was performed. In addition he had deep ulcers over both trochanters. His usual white blood cell count was 3,000 to 4,000. Routine urinalysis done in July and on Aug. 15, 1947 revealed no abnormalities.

On August 16 the patient complained of pain in the right lower quadrant. Tenderness was present. The white blood cell count was 6,550 with 52 per cent polymorphonuclear cells. Urinalysis showed 25 to 30 white blood cells, with a few red blood cells. Observation was decided on. On August 17 the temperature was 98.8 F., the tenderness in the right lower quadrant was more marked and some rebound tenderness was present. The patient was nauseated. The results of rectal examination were negative. The white blood cell count had risen to 8,400. In spite of the change in the urine, the surgeon who saw the patient elected to perform appendectomy for fear of neglecting acute appendicitis. The appendix was removed. It "did not look too bad." There was no Meckel diverticulum or enlarged lymph nodes in the mesentery. The pathologic report stated: "This section of appendix shows considerable fibrosis of the entire appendical wall, and there is some infiltration, especially of the serosal layer, with chronic inflammatory cells. The mucosa is almost entirely absent, and the lumen is filled with cellular debris and amorphous acidophilic material."

The postoperative course was uneventful. The sutures were removed on the fifth postoperative day. Although he has had no recurrence of the abdominal pain, nausea or relative leukocytosis since operation, he has had several instances of recurrence of cellular elements in the urine until the time of this writing, in March 1948.

CASE 2.—S. R., a 22 year old white man, suffered a fracture of the ninth thoracic vertebra on Aug. 29, 1945, which resulted in paralysis of the lower extremities, the sensory level at the tenth thoracic dermatome, and loss of bladder and rectal control. A urethral catheter was kept in place for bladder control. He was admitted to the Kennedy Veterans Administration Hospital on Aug. 24, 1946, with decubitus ulcers of the sacrum, hips, thighs, ankles and heels in addition to the aforementioned condition. Because of spasm, rhizotomy was performed on Sept. 10, 1946, including the anterior roots of the eleventh thoracic through the first sacral nerves and the posterior roots of the eleventh thoracic through the first lumbar nerves. Subsequently, acute pyelonephritis developed, which was successfully treated with penicillin and sulfadiazine. On Oct. 26 and Nov. 2, 1946, stones were removed from the bladder by cystoscopy. In the latter part of November 1947 another acute urinary infection occurred, which responded to penicillin. A dermanaplastic closure of the ulcer on the left side of the ischium was done on December 30 and redone on Jan. 30, 1947. On May 1, 1947, grafts were placed on the ulcers on the sacrum and the right trochanter.

On August 3 he began to complain of dull pain in the right lower quadrant. He had a white blood cell count of 10,000, with 72 per cent polymorphonuclear cells, slight elevation of the temperature and 10 to 20 white blood cells in the urine. Appendectomy was performed after several examinations revealed deep tenderness in the right lower quadrant. The pathologic report was lymphoid hyperplasia. The patient had no further bouts of pain.

In both instances the urologist, had he been called, could have corrected the complaints by treating the urinary infection. The surgeon was led to appendectomy in both of these cases, without acute appendicitis, because of the complaint of pain, the persistent tenderness and the elevated white blood cell count. It is difficult to criticize the removal of a nonsuppurative appendix in these cases when nonremoval of a suppurative appendix might lead to unrecognized perforation with its sad sequelae.

It has been a somewhat unexpected occurrence that in an average population of about 200 paraplegic patients at this hospital there have been no recognized instances of acute appendicitis in over one and one-half years of observation. Neither have any of the patients had peritonitis, which might have indicated inability to diagnose the condition.

CASE 3.—F. A., a 22 year old white man, suffered a fracture of the sixth cervical vertebra, with paralysis from the arm down, including the bowel and bladder, on Oct. 3, 1945, while wrestling and practicing jiu-jitsu. He was admitted to the Kennedy Army General Hospital on October 4. After traction, he could move his right arm somewhat. He improved gradually until he could move his legs and control urination with a condom-type apparatus by November 25 (automatic bladder). On Jan. 5, 1946, he was transferred to the Kennedy Veterans Administration Hospital. Examination showed chronic traumatic transverse incomplete myelitis, at the level of the first thoracic segment. In May 1946 he began to use his legs without a brace and was able to void without a catheter or the use of the condom some of the time. He required enemas for evacuation of the bowels. At no time did decubitus ulcers or urinary calculi develop.

On Nov. 4, 1947, he had an elevation of temperature to 100 F. and felt chilly. Subsequently he had similar elevations of temperature. The urine was normal. The lungs were clear. On November 18 a routine examination of the kidney, ureter and bladder showed no urinary calculi, but there were stones in the gallbladder. The white blood cell count at this time was 6,600 with 64 per cent polymorphonuclear cells. The prothrombin time was normal. An oral cholecystogram showed calculi in the gallbladder and the cystic duct. He had no pain during this period, and tenderness was not elicited. He had the common food likes and dislikes seen among paraplegic patients. There was no nausea or vomiting. Stools were of normal color. There being no other explanation of the fever, it was decided to do a cholecystectomy.

Cholecystectomy was done on Jan. 5, 1948, with the patient under cyclopropane anesthesia through a right rectus incision. Since the cholecystectomy was a simple one, routine appendectomy was done at the same time, and the gallbladder bed was drained. The common duct was found to be normal. There was a calculus in the cystic duct. The pathologic diagnosis was chronic cholecystitis with cholelithiasis and obliterative appendicitis. The drain was removed on the second postoperative day. The sutures were removed on the seventh postoperative day. An abdominal binder was used until the fifteenth postoperative day. Healing was per primum and uneventful. On the twenty-second day the patient was taken off the low fat diet and given the regular diet and routine daily enemas and placed on the rehabilitation program which he had been following prior to operation. When last seen, in March 1948, he was still afebrile.

CASE 4.—W. R., a 56 year old white man, suffered an injury to his right hip region in 1941, which left his right lower extremity weak. In 1944, while at work, he suddenly suffered paralysis of the lower half of the body, with numbness. In 1945 a laminectomy was performed and an epidural granuloma was removed from the region of the fifth thoracic vertebra. When he was admitted in 1947, studies revealed adhesive chronic arachnoiditis involving the fourth through the ninth thoracic segments due to epidural granuloma; transverse, chronic, incomplete, secondary myelitis, with paraplegia below the third thoracic segment and partial paralysis of the bowel and bladder, and psychoneurosis of the mixed type, with personality changes due to emotional instability and anxiety.

Beginning in June 1947, he complained of pain in the right upper quadrant, with radiation to the right scapula, along with many other aches and pains over the entire body, which were considered to be on a psychoneurotic basis. The pain in the right upper quadrant was often accompanied with pain in the left upper quadrant, which radiated much like symmetric root pain. In other words, his pain was difficult to evaluate. Neurologic, cardiac, colonic and genitourinary changes were ruled out by progressive studies and consultations. Four attempts at visualization of the gallbladder by the oral administration of priodax® (iodoalphonic acid N.N.R.) failed. His sensory level was complete just below the nipple line. In March 1946, because of the radiating pain and the nonfilling after dye was given orally, it was finally decided that he must have a diseased gallbladder, although localized tenderness or palpable viscus was not present. A history of intolerance to fatty foods could be elicited only to a minor degree. He did have belching and flatulence frequently. On many occasions he vomited, especially when he was emotionally upset.

On March 3, 1946, a celiotomy was done through a right rectus incision with the patient under anesthesia produced by cyclopropane given endotracheally and curare. A chronically inflamed gallbladder packed with cholesterol stones was found. The wall seemed thinned out by the numerous calculi. The common duct appeared normal. The gallbladder was removed, the bed of the viscus was drained and closure was performed in layers. Convalescence was uneventful. He was relieved of the pain and tenderness in the right upper quadrant, the belching and the flatulence, and he resumed his rehabilitation program.

It is felt by the surgical staff at this institution that the paraplegic patient with cholelithiasis should undergo cholecystectomy, even if the symptoms are mild, to avoid perforation or obstructive jaundice which might be difficult to recognize or to differentiate from hepatitis later. Because of the frequent association of cholecystitis with appendicitis, it is felt that when the cholecystectomy is a simple one, the appendix should be removed.

In case 3, because no other cause for the fever was found and to avoid later complications mentioned previously, it was decided to perform cholecystectomy although there was no pain or tenderness.

The psychoneurotic element, the bilateral pain and the absence of localized tenderness in case 4 were misleading, but, with suspicion aroused, the repeated nonfilling of the gallbladder after administration of dye finally led to cholecystectomy for a definitely diseased gallbladder.

CASE 5.—G. J., a 40 year old white man, fell down a flight of stairs on June 11, 1943, suffering cerebral concussion and fracture of the eleventh thoracic vertebra, resulting in complete motor and sensory paralysis below the level of the eleventh thoracic dermatome. Decubitus ulcers developed, and he had several attacks of pyelitis. Enemas were used for evacuation of the bowels, and urethral catheter with irrigations for control of the bladder.

Beginning in August 1945, he complained of pain in the lower abdominal area. This was not relieved by a chordotomy performed in 1946. In May 1947, shortly after an investigative cystoscopic examination, the pain became localized in the left lower quadrant, and he began to have mucopurulent, foul-smelling drainage from the rectum. His temperature rose to 100 or 101 F. daily. There was tenderness in the left lower quadrant. The results of examination after a barium enema were negative. The stools did not contain occult blood, amebas, ova or parasites. Proctosigmoidoscopic examination was noncontributory. The surgeon felt that there was an abscess in the left lower quadrant, possibly due to diverticulitis and recommended drainage. Further therapy with penicillin and streptomycin was elected, however. By June 10, 1947, a definite mass could be felt in the left lower quadrant laterally which was tender to palpation.

On June 24, 1947, exploration through a large left McBurney incision was done; inhalation anesthesia was used. A large abscess lateral to the sigmoid was found and drained. No evidence of the suspected diverticulitis was found. At no time was there any fecal drainage from the wound. His temperature rapidly became normal and the purulent drainage from the anus ceased. On July 7 the sutures in the skin were removed. Drainage from the incision gradually subsided and ceased, and the drain was removed. By July 22 he was well healed. Rehabilitation and treatment of his recurrent urinary infection and decubitus ulcers then proceeded as usual. A check barium enema revealed no diverticula or any other pathologic process, and pyelograms were normal. He has maintained this status to the time of this report, in March 1948.

The fever, the mucopurulent drainage from the rectum and the tenderness in the left lower quadrant in the absence of demonstrable ureteral calculus or lesion of the colon led the surgeon to suspect, correctly, the presence of pus under the area of tenderness. This patient feared carcinoma in spite of the assurance given after proctoscopic examination and study of the colon with barium gave negative results. The exploratory incision and the adequate drainage of the abscess relieved his mind and the condition causing symptoms.

CASE 6.—Z. J., a 25 year old white man, was struck by shell fragments in the spine on June 16, 1944, which resulted in complete transverse myelitis at the level of the tenth thoracic dermatome. Grafts were placed on a sacral ulcer in March 1945 and again in August 1945, finally resulting in healing. On Jan. 22, 1946, the suprapubic cystotomy opening was closed. In December 1945 chordotomy (second thoracic vertebra) was performed for pain.

While driving a "paraplegic automobile" on Aug. 13, 1947, the patient had an accident. He was brought to the hospital two hours later in a semiconscious state with lacerations about the face. Bowel sounds were diminished but present. Anesthesia was present below the tenth thoracic vertebra as before. There was no muscle spasm or rigidity, nor was there any distention. There was an obvious fracture of the right tibia. The knee region on both legs exhibited abnormal

mobility. There were numerous abrasions about the lower extremities. The blood pressure was 70 systolic. No diastolic pressure was elicited. The pulse was 140 per minute and the respiratory rate was 30 per minute. He was given 500 cc. of plasma and 500 cc. of citrated blood intravenously. His blood pressure fell to 50 systolic and 25 diastolic, and shifting dulness was elicited in the flanks. He complained of bilateral pain in the shoulder at this time. The abdomen became more tympanitic in the upper half, and the patient complained of severe thirst. At this time the temperature had risen to 104 F. Roentgenograms taken at the



Roentgenogram of chest, Aug. 24, 1947, showing elevation of the left side of the diaphragm in case 6.

bedside showed an oblique fracture through the shaft of the left tibia about 10 cm. from the knee joint. There were bilateral supracondylar impacted fractures through the distal ends of both femurs, with 1.5 cm. impaction on both sides.

In addition to the time taken for restorative measures there was several hours' delay in diagnosis because of the lack of local signs of intra-abdominal trauma and the lack of localizing tenderness and rigidity. However, the shock, the rapid pulse and the onset of pain in the left shoulder, which persisted after restorative measures were tried, along with the beginning distention and the shifting dulness led the surgeon to the conclusion that there was intra-abdominal bleeding, most probably from the spleen and less probably from torn mesentery.

Laparotomy was performed without anesthesia through a transverse incision in the upper abdominal area, at 5 a. m. Because of protrusion of the bowel in the wound, nitrous oxide-oxygen-ether anesthesia was started. Two thousand cubic centimeters of bloody fluid was aspirated from the peritoneal cavity. The spleen was lacerated at the hilus and contained a large subcapsular hemorrhage. It was removed. Closure was performed in layers with chromic surgical gut for the peritoneum and wire for the outer layers. Casts were applied to both lower extremities.

On the following day the distention seemed controlled by the Levine tube which had been inserted. Each day his temperature rose as high as 103 F. The urine was normal, and the output was good. He began to have diarrhea. The pulse rate increased gradually to 120 per minute and the leukocyte count was 27,000, with a shift to the left in the Schilling hemogram. The patient complained of pain in the left shoulder region. A roentgenogram showed the left leaf of the diaphragm to be elevated (figure). It was decided that he had a subphrenic abscess, and he was treated with streptomycin.

On Aug. 26, 1947, a portion of the tenth rib was resected posterolaterally and a pack placed against the diaphragmatic pleura. On August 29 the pack was removed and a large subphrenic abscess drained. After this the distention and diarrhea were alleviated. The temperature and the pulse rate gradually fell. On September 26 roentgenograms of the fracture sites showing good callus were obtained, and the casts were removed. The abscess gradually decreased in size, the administration of streptomycin was discontinued and by October 14 he was completely healed. Roentgenograms at this time showed the chest and diaphragm to be normal. Rehabilitation was then resumed and was being continued at the time of writing.

The diagnosis of the subphrenic abscess was more readily arrived at than that of splenic rupture. In addition to the fever and the referred pain in the left shoulder, which were suggestive, the elevated diaphragmatic leaf on the left made the diagnosis of subphrenic abscess conclusive.

#### COMMENT

It is being recognized that the paraplegic patients cannot be put away in bed and forgotten. Constant diligence is required to discover changes in their condition. The surgeon's role is to evaluate the signs, symptoms and accessory data properly and to follow through with adequate action based on good judgment. Complaints and changes in clinical status may be investigated by examinations and roentgenologic and laboratory studies as in other patients. The experience obtained from this small group of cases as well as from others in which colostomy and colostomy closure were done for traumatic abdominal conditions seems to indicate that the patients withstand abdominal surgery well and that healing progresses as usual, providing nutrition, fluid balance and circulating blood elements are kept within normal limits by the usual methods.

No doubt there will be other abdominal conditions arising which will require thought and action on the part of the general surgeon. It is

the practice of the paraplegic service at this hospital to make periodic surveys of these patients, including flat roentgenograms of the abdomen, blood counts and urinalyses. All patients are kept on adequate diets and urinary infection and calculi are kept at a minimum with the use of acidification, antibacterial agents, ambulation and surgical intervention. The surveys act as a base line for changes when complaints develop which require surgical judgment. Unquestionably, it is difficult, even with this help, to be as certain as with normal subjects.

#### SUMMARY

Signs and symptoms of abdominal conditions requiring surgical treatment in patients with chronic paraplegia are discussed.

Two cases involving the appendix, 2 cases of cholelithiasis, 1 of perisigmoid abscess and 1 of a traumatic spleen complicated by a postoperative subphrenic abscess are presented.

Routine clinical and laboratory surveys as well as diligent "search for trouble" are valuable in determining abdominal conditions in patients with chronic paraplegia.

Experience with this small group of cases seems to indicate that patients with chronic paraplegia withstand abdominal operations well and heal as quickly as others do.



# ADENOMATOUS GOITERS WITH AND WITHOUT HYPERTHYROIDISM

Some Aspects of the Relationship of the Microscopic Appearance to Hyperthyroidism

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THE DATA presented herein are drawn from a larger study. The general purpose of the complete study was to determine if possible whether any histologic data can be found on the adenomatous nodules of the thyroid gland which would correlate with the presence of thyrotoxicosis in a patient. In short, it was decided to inquire again into the question of whether the pathologist can predict the presence of toxic phenomena in the patient from examination of the nodular or adenomatous tissue from the thyroid gland.

A nodule of the thyroid gland may be defined as a more or less encapsulated mass of thyroid tissue which may or may not be different from the surrounding thyroid tissue.

The term "nodular goiter" is used frequently by pathologists and surgeons as a synonym for adenomatous goiter. Although it is true that adenomatous goiters are nodular, thyroid nodules are not necessarily adenomas. Thyroid nodules may be composed of apparently normal thyroid tissue, colloid, inflammatory or lymphoid tissue, adenomas or carcinomas (figs. 1 and 2).

## THE ADENOMA

Adenomas of the thyroid gland are encapsulated and differ macroscopically and microscopically from the surrounding thyroid tissue. Adenomas may be single or multiple and may be associated with hyperthyroidism, with normal or reduced thyroid function or with exophthalmic goiter. They tend to undergo degeneration, such as necrosis, hemorrhage, fibrosis, hyalinization, calcification, formation of cysts and lipoidosis. Degenerative changes are more marked in the adenoma than in the extra-adenomatous thyroid tissue.

Adenomas usually contain follicles of fetal type and larger follicles containing colloid. However, the cells may appear (1) in diffuse

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masses without formation of follicles (undifferentiated fetal adenoma); (2) in small follicles of fetal type with small lumens which contain no colloid (fetal adenoma); (3) in follicles of fetal type with larger lumens and a small colloid content, or (4) in well developed follicles lined by cuboid or columnar epithelium and with large lumens filled with colloid (fetal and colloid adenoma).<sup>1</sup> Unencapsulated nodules which consist only of thyroid tissue containing colloid are not regarded as true adenomas but as part of a colloid goiter.

Opinions differ about the microscopic appearance of thyroid adenomas removed from patients with clinical manifestations, which H. S. Plummer<sup>2</sup> designated adenomatous goiter with hyperthyroidism.



Fig. 1.—Multiple well encapsulated adenomas of the thyroid.

Broders<sup>3</sup> has stated that the amount and height of the columnar epithelium in the adenomas (parenchymatous hypertrophy) probably

1. Broders, A. C., and Parkhill, E. M.: Symposium on Surgical Lesions of Thyroid: Diffuse and Adenomatous Goiter and Goiter Induced by Various Agents, *Surgery* **16**:633-646 (Nov.) 1944.

2. Plummer, H. S.: The Clinical and Pathologic Relationships of Hyperplastic and Non-Hyperplastic Goiter, *J. A. M. A.* **61**:650-651 (Aug. 30) 1913.

3. Broders, A. C.: Personal communication to the author; *Surgical Pathology of the Thyroid Gland*, *West. J. Surg.* **48**:620-632 (Oct.) 1940. Broders and Parkhill.<sup>1</sup>

determine the activity of thyroid adenomas. In order to make a diagnosis of adenomatous goiter with hyperthyroidism on microscopic examination he requires that the extra-adenomatous thyroid tissue be practically normal or at least not show the microscopic features of exophthalmic goiter.

Broders<sup>3</sup> has found that intra-adenomatous columnar epithelium, with or without papillary infolding, appears most often in adenomas associated with exophthalmic goiter, less often in adenomas associated with hyperthyroidism and rarely or perhaps one should say least often, in adenomas from patients with normal thyroid function.



Fig. 2.—Small noncapsulated colloid nodule from a thyroid gland, not an adenoma;  $\times 13$ .

Welch and Broders<sup>4</sup> studied the Golgi apparatus in the thyroid glands of 73 patients. Thirty-five of the patients had exophthalmic goiter, 21 adenomatous goiter with clinical hyperthyroidism, 16 adenomatous goiter in which clinical hyperthyroidism was not evident and 1 colloid goiter. Of the 35 glands examined from patients with exophthalmic goiter, 34 showed hypertrophy of the Golgi apparatus. Of

4. Welch, C. S., and Broders, A. C.: Golgi Apparatus of the Thyroid Gland, *Arch. Path.* 29:759-772 (June) 1940.

the 21 adenomatous thyroid glands examined in which the patients had clinical hyperthyroidism, only 7 had intra-adenomatous cellular hypertrophy, whereas 19 had a hypertrophied Golgi apparatus, which led the authors to suggest that the size of the Golgi apparatus is a more delicate method of estimating cellular function than the usual histologic one. Of the 16 adenomatous thyroid glands from patients who did not have clinical evidence of hyperthyroidism, only 1 showed intra-adenomatous cellular hypertrophy and 5 showed hypertrophy of the Golgi apparatus. In colloid goiter the Golgi apparatus was not enlarged.

Before the use of iodine in the treatment of hyperthyroidism, Wilson<sup>5</sup> studied a large number of adenomatous goiters without diffuse extra-adenomatous parenchymatous hypertrophy and hyperplasia. He found that in 90 per cent of the group in which a clinical diagnosis of hyperthyroidism was made, small areas of either intra-adenomatous or extra-adenomatous hypertrophy and hyperplasia were present. In 95 per cent of the nonhyperthyroid group, no areas of parenchymatous hypertrophy and hyperplasia were found. The hypertrophy and hyperplasia were often so moderate in degree and amount as to escape notice except by careful inspection. The most pronounced evidence of hypertrophy and hyperplasia in adenomatous goiter with hyperthyroidism was comparable to that in untreated exophthalmic goiter of the mildest degree.

Rice<sup>6</sup> stated that the histologic diagnosis of adenomatous goiter with hyperthyroidism is an uncertainty. Only 58 per cent of the adenomas with hyperthyroidism that he examined showed evidence of parenchymatous hypertrophy and hyperplasia.

A number of writers have found it impossible microscopically to distinguish between thyroid adenomas with hyperthyroidism and those without it.<sup>7</sup> Although formerly hypertrophy and hyperplasia in the

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5. Wilson, L. B.: A Study of the Pathology of the Thyroids from Cases of Toxic Non-Exophthalmic Goiter, *Am. J. M. Sc.* **147**:344-351 (March) 1914; The Pathology of Nodular (Adenomatous?) Goiters in Patients With and in Those Without Symptoms of Hyperthyroidism, *Am. J. M. Sc.* **165**:738-742 (May) 1923.

6. Rice, C. O.: Exophthalmic Goiter Versus Toxic Adenoma: Clinical and Pathologic Differential Features, *Minnesota Med.* **17**:361-365 (June) 1934.

7. (a) Marine, D., and Lenhart, C. H.: The Pathological Anatomy of the Human Thyroid Gland, *Arch. Int. Med.* **7**:506-535 (April) 1911. (b) Graham, A.: Exophthalmic Goiter and Toxic Adenoma: Clinical Variations of the Same Disease, *J. A. M. A.* **87**:628-631 (Aug. 28) 1926. (c) Marine, D., and Lenhart, C. H.: On the Occurrence of Goitre (Active Thyroid Hyperplasia) in Fish, *Bull. Johns Hopkins Hosp.* **21**:95-98 (April) 1910. (d) Rienhoff, W. F., Jr., and Lewis, D.: Relation of Hyperthyroidism to Benign Tumors of the Thyroid Gland, *Arch. Surg.* **16**:79-116 (Jan.) 1928. (e) Bovi, E. J. D.: Thyroid Gland: A Clinical Pathologic Study with Special Reference to True Tumor: Analysis of Two Hun-

thyroid have often been taken as evidence of hyperfunction, certain goitrogenic substances, for example cabbage, potassium thiocyanate, sulfonamide drugs and thiouracil, have been shown to produce notable degrees of hypertrophy in the thyroid, with diminished thyroid function.<sup>8</sup> While the effect of such substances on the microscopic appearance of thyroid nodules has not been fully established, it must be kept in mind in any consideration of the significance of hypertrophy of thyroid cells.

Adenomatous goiters may occur in cretins, and Hertzler<sup>9</sup> designated them as bosselated congenital goiters. "Cross section of these degenerated goiters presents a general pattern of diffuse, small cystic degeneration with multiple fetal adenomatosis. The microscopic picture varies. For the most part, there is an absence of colloid. Usually the epithelium is cuboid."

#### MATERIAL STUDIED AND METHOD

For this study material was obtained at necropsy and at operation on the thyroid gland. The necropsy material consisted of 165 thyroid glands. These were completely removed at necropsy during a six month period at the Mayo Clinic. In each case the patient died of a disease not primarily related to the thyroid gland. The surgical material consisted of 58 adenomatous goiters without hyperthyroidism and 115 adenomatous goiters with hyperthyroidism. These goiters were selected from a consecutive group, surgically removed. All cases of carcinoma of the thyroid were excluded from the surgical series. In each of the 58 cases a consultant in the Section on Metabolism of the Mayo Clinic had made a clinical diagnosis of adenomatous goiter without hyperthyroidism, and in each of the 115 cases one had made a clinical diagnosis of adenomatous goiter with hyperthyroidism.

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dred and Sixteen Cases, *Arch. Surg.* **39**:624-636 (Oct.) 1939. (f) Warwick, M.: The Pathology of Toxic Goiter, *Minnesota Med.* **10**:411-412 (July) 1927. (g) Enzer, N.: The Pathology of Nodular Goiter, *Ann. Int. Med.* **3**:1241-1251 (June) 1930. (h) Boyd, A. M.: The Pathology of Single Nodule of the Thyroid Gland, *Brit. J. Surg.* **25**:782-789 (April) 1938.

8. Chesney, A. M.; Clawson, T. A., and Webster, B.: Endemic Goitre in Rabbits, *Bull. Johns Hopkins Hosp.* **43**:261-277 (Nov.) 1928. Rawson, R. W.; Hertz, S., and Means, J. H.: Thiocyanate Goiter in Man, *Ann. Int. Med.* **19**:829-842 (Dec.) 1943. Webster, B., and Chesney, A. M.: Endemic Goitre in Rabbits, *Bull. Johns Hopkins Hosp.* **43**:291-308 (Nov.) 1928. MacKenzie, C. G., and MacKenzie, J. B.: Effect of Sulfonamides and Thiourea on the Thyroid Gland and Basal Metabolism, *Endocrinology* **32**:185-209 (Feb.) 1943. Astwood, E. B.; Sullivan, J.; Bissell, A., and Tyslowitz, R.: Action of Certain Sulfonamides and of Thiourea on the Function of the Thyroid Gland of the Rat, *Endocrinology* **32**:210-225 (Feb.) 1943. Marine and Lenhart.<sup>7c</sup> Rienhoff and Lewis.<sup>7d</sup> Bovi.<sup>7e</sup>

9. Hertzler, A. E.: Diseases of the Thyroid Gland Presenting the Experience of More than Forty Years, New York, Paul B. Hoeber, Inc., 1941.

The surgical series was carefully selected in order to exclude any gland in which the extra-adenomatous parenchymatous hypertrophy was more than grade 1. The basis of grading will be described later. This selection was made in order to find out whether in adenomatous goiters the grade of intra-adenomatous parenchymatous hypertrophy correlated with the presence and degree of hyperthyroidism.

The age and sex of each patient whose thyroid was studied, the weight of each thyroid gland, the presence of nodules and adenomas, the microscopic appearance of the thyroid, the presence and grade of intra-adenomatous and extra-adenomatous parenchymatous hypertrophy and the significant clinical and pathologic findings were recorded. Each thyroid was sectioned every 2 to 3 mm. on gross examination in a search for adenomas. Other details in the study and selection of necropsy and surgical material were as follows: Blocks from the 58 surgically removed thyroids were embedded in paraffin; sections were taken from each block and stained with hematoxylin and eosin.

In a few instances the adenoma was largely calcified, and it was possible to get only a few sections. When extra-adenomatous tissue was present, sections were made of this to rule out diffuse parenchymatous hypertrophy.

The 115 surgically removed thyroids in cases in which the clinical diagnosis of adenomatous goiter with hyperthyroidism was made and the 165 thyroids removed at necropsy were sectioned in the same manner.

In this study, parenchymatous hypertrophy is defined as a change in the thyroid follicular cells from flat or cuboid epithelium to columnar epithelium. The extent of parenchymatous hypertrophy was graded from 0 to 4, grade 0 representing a gland with minimal or no columnar epithelium and grade 1 a gland with low columnar epithelium in at least several areas in a section. Grade 4 indicated the presence of diffuse high columnar epithelium, corresponding to the usual histologic picture in untreated exophthalmic goiter, and grades 2 and 3 were intermediate between grades 1 and 4 (figs. 3 to 6).

The grade of parenchymatous hypertrophy recorded was the highest found in any one section. A large number of sections was cut from each gland. A thyroid showing extra-adenomatous parenchymatous hypertrophy greater than grade 1 (on a basis of 1 to 4, in which 1 represents the least and 4 the greatest degree) was considered to be possibly an exophthalmic goiter and was therefore excluded from the surgical group.

#### OBSERVATIONS IN NECROPSY GROUP

Of the 165 thyroid glands removed at necropsy, 97 (58.8 per cent) were nodular. Forty-nine (50.5 per cent) of the nodular goiters were adenomatous goiters. The remaining nodules were found to be adult

thyroid tissue, colloid cysts, colloid nodules or inflammatory thyroid tissue. Three (6.1 per cent) glands in this group were substernal.

*Age of Patients.*—The average age of the 68 patients in this group who had apparently normal thyroid glands, that is, without nodules, was 51.8 years; the age of those who had nodular thyroids without adenomas was 57.1 years and of those who had adenomatous goiters 65.4 years. No adenomas were found in patients less than 20 years of age. In this group the incidence of nodular goiters seemed to increase with age.



Fig. 3.—Two fetal and colloid adenomas of the thyroid gland separated by a fibrous capsule. Intra-adenomatous parenchymatous hypertrophy of grade 0;  $\times 55$ .

*Sex.*—Of the 165 persons examined at necropsy, 115 were men. Sixty-six (57.4 per cent) of these had nodular goiters. Twenty-five (21.7 per cent of the men, or 37.9 per cent of the men who had nodular goiters) had adenomatous goiters. Of the 50 women in this group, 33 (66 per cent) had nodular goiters and 23 (46 per cent of the total number of women, or 70 per cent of the women with nodular goiters) had adenomatous goiters. The incidence of small thyroid nodules was about 10 per cent greater in women than in men, and the incidence of small adenomatous goiters was more than twice as high in women.

*Weight.*—The average weight of the thyroid glands without nodules removed at necropsy was 26 Gm. The weight varied from 5 to 61 Gm. The smallest thyroid was removed from a patient who had hypopituitarism. The average weight of the nodular thyroids without adenomas removed at necropsy was 28 Gm.; the weight ranged from 10 to 52 Gm. The average weight of the 49 adenomatous thyroids removed at necropsy was 48.5 Gm. The smallest, which was from a patient who previously had undergone subtotal thyroidectomy, weighed 8 Gm. and the largest 232 Gm.



Fig. 4.—Intra-adenomatous parenchymatous hypertrophy of the thyroid of grade 1;  $\times 160$ .

*Microscopic Observations.*—Of the 49 adenomatous goiters encountered at necropsy, in 2 (4 per cent) unsuspected adenocarcinoma, grade 4, was found. In 15 (30.6 per cent) there was intra-adenomatous parenchymatous hypertrophy of more than grade 1. Some of these also showed extra-adenomatous parenchymatous hypertrophy. This may indicate the existence of exophthalmic goiter. Thirty-seven (75.5 per cent) showed degenerative changes, that is, hemorrhage, fibrosis, hyalinization, cyst formation, lymphocytic infiltration, deposits of cholesterol



crystals and lipid granular degeneration. Four (8.2 per cent) were pure fetal adenomas. The other 45 (91.8 per cent) were fetal and colloid adenomas.

#### SURGICAL SERIES

The basal metabolic rate before operation ranged from  $-20$  to  $+10$  per cent in the 58 cases of adenomatous goiter without hyperthyroidism and from  $+11$  to  $+93$  per cent in the 115 cases of adenomatous goiter with hyperthyroidism. Three (5.2 per cent) of the adenomatous goiters



Fig. 5.—Intra-adenomatous parenchymatous hypertrophy of the thyroid of grade 2;  $\times 160$ .

without hyperthyroidism in the surgical series were substernal and 8 (7 per cent) of the adenomatous goiters with hyperthyroidism were substernal.

*Age of Patient.*—The average age at the time of operation of the patients in this series who had undergone surgical resection of adenomatous goiters without hyperthyroidism was 47.5 years. For those who had had adenomatous goiters with hyperthyroidism surgically removed the average age was 51.4 years. There was no patient in this series less than 20 years of age with an adenomatous goiter.

Only 15 per cent of the patients who had undergone surgical resection of adenomatous goiters with hyperthyroidism were less than 40 years old. Five (8.6 per cent) of those with adenomatous goiters without hyperthyroidism were more than 60 years old, while 32 (27.8 per cent) of those with adenomatous goiters with hyperthyroidism were more than 60. Of the patients who were more than 60 years old and had had adenomatous thyroid resected, 82.1 per cent had hyperthyroidism.

*Sex.*—Of the 58 adenomatous goiters without hyperthyroidism removed by subtotal resection, 51 (87.9 per cent) were from women. Of



Fig. 6.—Intra-adenomatous parenchymatous hypertrophy of the thyroid of grade 2 to 3;  $\times 360$ .

the 115 adenomatous goiters with hyperthyroidism surgically removed, 93 (80.8 per cent) were from women. In this series, therefore, adenomatous goiters of sufficient size or producing symptoms sufficient to bring the patient to operation were four to seven times as common in women as in men.

*Weight.*—The average weight of the surgically resected adenomatous goiters without hyperthyroidism was 88.7 Gm. The smallest amount of thyroid tissue removed was 13 Gm. and the largest amount 390 Gm.

The average weight of the surgically resected adenomatous goiters with hyperthyroidism was 92 Gm. The smallest amount of thyroid tissue removed was 16 Gm. and the largest amount 632 Gm.

*Microscopic Observations.*—That degenerative changes are common in thyroid adenomas is shown by their occurrence in 100 per cent of those removed surgically. In 11 (19 per cent) of the 58 cases of adenomatous goiter without hyperthyroidism intra-adenomatous parenchymatous hypertrophy was graded 1. In no case was the parenchymatous hypertrophy found to be greater than grade 1. Thus in 81 per cent of the nontoxic adenomas minimal or no columnar epithelium was present.

*Relationship of Basal Metabolic Rate to Intra-Adenomatous Hypertrophy:  
Data from Surgical Series*

Basal Metabolic Rate, Percentage	Total Cases	Intra-Adenomatous Hypertrophy				Present; Percentage of Total
		None Present (Grade 0)	Grade			
			One	Two	Three	
−20 to −10.....	14	11	3	..	..	21
− 9 to 0.....	26	22	4	..	..	15
+ 1 to +10.....	18	14	4	..	..	22
+11 to +20.....	19	12	4	3	..	37
+21 to +30.....	36	24	10	1	1	33
+31 to +40.....	39	26	8	3	2	33
+41 to +50.....	10	5	3	2	..	50
+51 to +60.....	8	2	4	2	..	75
+61 to +70.....	1	1	..	..	..	0
+71 to +80.....	1	1	..	..	..	0
+81 to +90.....	0	..	..	..	..	..
+91 to +100.....	1	1	..	..	..	0

In 43 (37 per cent) of the 115 adenomas with hyperthyroidism, intra-adenomatous parenchymatous hypertrophy was found. In 29 cases (25 per cent) the intra-adenomatous parenchymatous hypertrophy was grade 1, in 11 cases (10 per cent) it was grade 2 and in 3 cases (3 per cent) it was grade 3. In no case was it graded 4. In 72 cases minimal or no columnar epithelium was found (table).

The table demonstrates that some correlation exists between the degree of hyperthyroidism and the presence of intra-adenomatous parenchymatous hypertrophy in this series in which the clinical diagnosis was adenoma of the thyroid gland with or without hyperthyroidism.

COMMENT AND SUMMARY

Tissue from 338 thyroid glands was studied. This consisted of tissue from 165 thyroid glands obtained at necropsy in a period of six months and of thyroid tissue removed at operation in 58 cases of

adenomatous goiter without hyperthyroidism and in 115 cases of adenomatous goiter with hyperthyroidism. It was required for inclusion in the study that the extra-adenomatous thyroid tissue in the surgically removed glands should not have the histologic picture of exophthalmic goiter, that is, parenchymatous hypertrophy of more than grade 1. This restriction on selection of cases made it reasonably certain that cases of adenomatous goiter with and without hyperthyroidism were studied in almost all instances. The adenomatous goiters in the surgical series were, on an average, much larger than those removed at necropsy, and the average age of the subjects was considerably less. The study of the necropsy material indicated that nodular thyroid tissue did not greatly increase the average weight of the thyroid gland unless the nodules were adenomas. The large thyroid nodules were usually adenomas. From the surgical series it would appear that the presence of hyperthyroidism does not greatly increase the average weight of adenomatous goiters and the size of the adenoma cannot be correlated with hyperthyroidism in this series.

The sex incidence of adenomatous goiter in this series is of interest. In the necropsy group 22 per cent of the men and 46 per cent of the women had adenomatous goiters. In the surgical series in this group of patients who had adenomatous goiter without hyperthyroidism 12 per cent were men and 88 per cent were women; in the group of patients with hyperthyroidism 20 per cent were men and 80 per cent women. However, the total number of patients included in the entire series is rather small for statistical analysis.

Analysis of the necropsy material revealed that 4 per cent of the adenomas contained malignant growths. This observation might be pertinent in indicating whether a small adenoma should be removed surgically.

In the study of the surgical material intra-adenomatous parenchymatous hypertrophy, grade 1, was encountered in approximately a fifth of the cases of adenomatous goiters without hyperthyroidism. In the other four fifths of the cases there was no intra-adenomatous parenchymatous hypertrophy.

In the adenomatous goiters with hyperthyroidism surgically removed, intra-adenomatous parenchymatous hypertrophy was present in nearly two fifths of the cases. In about a third of these the intra-adenomatous parenchymatous hypertrophy present was higher than grade 1.

In the surgical series some correlation was found to exist between the frequency of occurrence of intra-adenomatous parenchymatous hypertrophy and the degree of hyperthyroidism.

## REGULATION OF LONGITUDINAL BONE GROWTH

STERLING G. PARKER, M.D.

DECATUR, ILL.

THE MECHANISM of control of individual stature has been a subject for extensive research and conjecture for two centuries or more, and yet it is little understood. Growth is an inherent property of living matter, but the regulation of growth is under more specific controls which can be altered by chemical or other means that disturb the normal physiologic balance of tissue metabolism. If we could fully understand these factors, then we should be able to govern skeletal growth, to some extent at least, of normal growing people and to alter the course of pathologic growth when it is produced by physiologic imbalances.

It is well known that many factors can stimulate, inhibit or halt longitudinal bone growth in a given bone or extremity, depending on the mechanism involved. In general, conditions which produce hyperemia, and hence increase metabolic activity of the part, produce an increased rate of longitudinal bone growth during the period that the hyperemia exists.<sup>1</sup> Processes which decrease local metabolism<sup>2</sup> or interfere with the normal influence of stress or strain<sup>3</sup> slow longitudinal skeletal growth of the involved extremity, and anything which destroys the epiphysal cartilage will, of course, halt growth at that epiphysis permanently. It is also well known that nutritional deficiencies can cause gross disturbances of growth, which are pathologic states only to be considered here as they may be related to an understanding of normal bone growth. Congenital and acquired disorders will likewise be described only when they are helpful in clarifying the mechanism of regulation of growth.

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2. Armstrong, W. D.: Bone Growth in Paralyzed Limbs, *Proc. Soc. Exper. Biol. & Med.* **61**:358, 1946.

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## HISTORICAL OBSERVATION

Stephen Hales <sup>4</sup> in 1727 scientifically recorded his observations on bone growth and thus initiated a study which has since grown in scope and magnitude. Using a half-grown chick, he pierced two holes in its legs at a measured distance with a sharp-pointed iron and found that two months later the marks were still equidistant, although the leg had grown 1 inch (2.54 cm.) in length. He concluded that this growth in length was from the epiphysis and that proper nutritive matter was necessary for its growth. Duhamel <sup>5</sup> confirmed this in 1743 in the pigeon and in the dog. The classic experiments of John Hunter <sup>6</sup> showed more accurately that normal longitudinal growth of the shaft of a long bone occurred only at the epiphysis. Also, by using Belchier's observation <sup>7</sup> that animals fed on madder root had a red tinge to their bones, he showed that the increase in diameter of bone was due to new bone being formed on the exterior of the shaft. These conclusions have been confirmed by Compere,<sup>1a</sup> Müsenbach,<sup>1b</sup> Humphry,<sup>8</sup> Wegner,<sup>9</sup> Haas,<sup>10</sup> Gatewood and Mullen <sup>11</sup> Payton,<sup>12</sup> Selye,<sup>13</sup> Phemister,<sup>14</sup> Bisgard and Bisgard,<sup>15</sup> Siegling,<sup>16</sup> and Aries.<sup>17</sup> From

4. Hales, S.: *Statical Essays*, London, W. Innys [and others], 1727, vol. 1, p. 339.

5. Duhamel, H. L.: *Cinquieme memoire sur les os*, *Mém. Acad. Roy. d. Sc.*, 1743, p. 111, cited by Humphry.<sup>8</sup>

6. Hunter, J.: *Experiments and Observations on the Growth of Bones*, from the Papers of the Late Mr. Hunter with Notes, edited by James F. Palmer, 1835, vol. 4, p. 315.

7. Belchier, J.: *An Account of the Bones of Animals Being Changed to a Red Colour by Aliment Only*, *Phil. Tr.*, London **39**:287, 1736.

8. Humphry, G. M.: *Observations on the Growth of Long Bones and of Stumps*, *Med.-Chir. Tr.*, London **44**:117, 1861.

9. Wegner, G.: *Ueber das normale und pathologische Wachstum der Röhrenknochen*, *Virchows Arch. f. path. Anat.* **61**:44, 1874.

10. Haas, S. L.: *Interstitial Growth in Growing Long Bones*, *Arch. Surg.* **12**:887 (April) 1926.

11. Gatewood, M. D., and Mullen, B. P.: *Experimental Observations on the Growth of Long Bones*, *Arch. Surg.* **15**:215 (Aug.) 1927.

12. Payton, C. G.: *The Growth in Length of the Long Bones in the Madder-Fed Pigs*, *J. Anat.* **66**:414, 1932.

13. Selye, H.: *On the Mechanism Controlling the Growth in Length of the Long Bones*, *J. Anat.* **68**:289, 1934.

14. Phemister, D. B.: *Bone Growth and Repair*, *Ann. Surg.* **102**:261, 1935.

15. Bisgard, J. D., and Bisgard, M. E.: *Longitudinal Growth of Long Bones*, *Arch. Surg.* **31**:568 (Oct.) 1935.

16. Siegling, J. A.: *Growth of the Epiphyses*, *J. Bone & Joint Surg.* **23**:23, 1941.

17. Aries, L. J.: *Experimental Analysis of the Growth Pattern and Rates of Appositional and Longitudinal Growth in the Rat Femur*, *Surg., Gynec. & Obst.* **72**:679, 1941.

these studies it can be said positively that normal longitudinal growth of the shaft occurs only at the epiphysis. That this growth is from the diaphysial side of the epiphysis was further shown by Brücke,<sup>18</sup> who rotated the epiphysial cartilages in rabbits 180 degrees, demonstrating that bony apposition took place only on the side originally facing the diaphysis.

With the advent of the science of endocrinology, certain disturbances of skeletal growth were suspected of being associated with dysfunctions of the ductless glands, although Marie,<sup>19</sup> in a classic description of acromegaly in 1889, stated that the etiology of acromegaly was unknown but that certain cases could be attributed to syphilis. Massalongo<sup>20</sup> in 1892 attributed acromegaly to hyperfunction of the pituitary gland, and Furnivall<sup>21</sup> in 1898 collected 49 cases of acromegaly in all but 2 of which there were abnormalities of the pituitary gland at autopsy. Benda<sup>22</sup> in 1900 found that the element chiefly concerned in the hyperplasia of the pituitary was the eosinophilic cells, and Lewis<sup>23</sup> in 1905 found similar changes. Casseli<sup>24</sup> in 1900 was the first to note a suggestive retardation of development after hypophysectomy. This was shown conclusively by Crowe, Cushing and Homans in 1910<sup>25</sup> and later by Aschnan<sup>26</sup> and Smith,<sup>27</sup> the latter also noting that there was atrophy of the thyroid and gonads as well as retardation of growth.

18. Brücke, F.: Zur Frage der Bedeutung des Epiphysenfugenknorpels für das Wachstum der langen Röhrenknochen, *Virchows Arch. f. path. Anat.* **279**:641, 1931.

19. Marie, P.: Acromegaly, *Brain* **12**:59, 1889.

20. Massalongo, R.: Sull' acromegalia, *Riforma med.* **8**:76 and 87, 1892.

21. Furnivall, P.: Pathological Report on a Case of Acromegaly, with the Analysis of the Results of Forty-Nine Post-Mortem Examinations on Cases of Acromegaly, *J. Path. Soc., London* **49**:204, 1898.

22. Benda, C.: Beiträge zur normalen und pathologischen Histologie der menschlichen Hypophysis cerebri, *Klin. Wchnschr.* **37**:1205, 1900.

23. Lewis, D. D.: Hyperplasia of the Chromophile Cells of the Hypophysis as the Cause of Acromegaly with Report of a Case, *Bull. Johns Hopkins Hosp.* **16**:157, 1905.

24. Caselli, A.: Influenza della funzione dell' ipofisi sulla sviluppo dell' organismo, nota preventiva sulla fisio-patologia della ghiandola pituitaria, *Riv. sper di freniat., Reggio-Emilia*, **176**:486, 1900.

25. Crowe, S. J.; Cushing, H., and Homans, J.: Experimental Hypophysectomy, *Bull. Johns Hopkins Hosp.* **21**:127, 1910.

26. Aschnan, B.: Pfüger's *Arch. f. d. ges. Physiol.* **146**:1, cited by Eaton, J. C.: The Influence of the Endocrines on the Skeleton, *Glasgow M. J.* **27**:93, 1946.

27. P. E.: Experimental Ablation of the Hypophysis in the Frog **44**:280, 1916.

Early investigators,<sup>28</sup> in an attempt to identify a specific function of the pituitary gland, fed fresh tissue to animals without any effect except questionable retardation of growth. They also used alcoholic extracts, without any definite conclusions. In 1921 Evans and Long<sup>29</sup> prepared an alcoholic extract of fresh pituitary glands, which was injected into rats intraperitoneally. They noted a consistent increased rate of growth in the experimental animals. In the treated animals a mild degree of gigantism was produced; the rats grew to twice the size of controls. In these animals the skeleton was invariably larger and heavier. Later they showed that the substance was not effective when administered orally.<sup>30</sup> These experiments formed the basis for the identification of the pituitary gland as the organ occupying the highest position in the endocrine order of growth regulators.

The relationship of the thyroid gland to skeletal growth was noted early in the history of endocrinology. Von Eiselberg<sup>31</sup> obtained stunting in goats subsequent to removal of the thyroid gland in 1894, and Langhans<sup>32</sup> described the changes occurring in the cretin, noting the small, indistinct cells of the epiphysial cartilage. MacCallum<sup>33</sup> described in accurate detail the anatomy of the myxedematous idiot in whom aplasia of the thyroid, gonad infantilism and hypertrophy of the hypophysis were found. He concluded that it was a general nutritional disturbance secondary to the thyroid aplasia. That other glands were also related to skeletal growth was demonstrated by Poncet<sup>34</sup> and Sellheim,<sup>35</sup> who were the first to demonstrate experimentally the delay-

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28. Aldrich, T. B.: On Feeding Young White Rats the Posterior and the Anterior Parts of the Pituitary Gland, *Am. J. Physiol.* **31**:94, 1912. Robertson, T. B.: The Influence of Tethelin, the Growth-Controlling Principle of the Anterior Lobe of the Pituitary Body, upon the Growth of the White Mouse, *J. Biol. Chem.* **24**:397, 1916. Robertson, T. B.: The Influence of the Anterior Lobe of the Pituitary Body upon the Growth of the White Mouse, *ibid.* **24**:385, 1916.

29. Evans, H. M., and Long, J. A.: The Effects of the Anterior Lobe Administered Intraperitoneally upon Growth, Maturity and Oestrous Cycles of the Rat, *Anat. Rec.* **21**:62, 1921.

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31. Von Eiselberg, A.: *Arch. f. Klin. Chir.* **49**:207, 1897.

32. Langhans, T.: Anatomische Beiträge zur Kenntniss der Cretinen, *Arch. f. path. Anat. u. Physiol.* **149**:155, 1897.

33. MacCallum, W. G., and Fabyan, M.: On the Anatomy of a Myxoedematous Idiot, *Johns Hopkins Hosp. Bull.* **18**:341, 1907.

34. Poncet, A.: De l'influence de la castration sur le developpement du squelette, recherches experimentales et cliniques, *Compt. rend. Soc. de biol.* **55**:65, 1903.

35. Sellheim, H.: Kastration und Knochenwachstum, *Beitr. z. Geburtsh. u. Gynäk.* **2**:236, 1899.



ing effect of castration on epiphysiodiaphysial union and noted that natural castration in human beings resulted in consistent increases in average skeletal height.

#### EFFECTS OF THE ANTERIOR LOBE OF THE PITUITARY ON BONE GROWTH

*Removal of the Anterior Lobe.*—In growing rats most investigators have found an immediate and complete cessation of growth after total hypophysectomy.<sup>36</sup> In puppies almost total cessation of growth is seen soon after total hypophysectomy,<sup>37</sup> but Reichert and Dandy<sup>37a, b</sup> showed that there was slight but definite skeletal growth after the removal of the pituitary for a period of two or three weeks in contrast to the immediate cessation of growth observed in rats. This could theoretically be explained by the presence of residual hormone. The epiphysial lines remained open in these puppies without evidence of closure long after closure had occurred in the controls. Another uniform finding after hypophysectomy has been the decrease in the appetite of the animal, but it is only recently that this has been accurately correlated with the changes in growth. Samuels<sup>38</sup> showed that hypophysectomized rats which were fed by stomach tube a diet sufficient to maintain growth in controls would continue to gain weight at a diminished rate. They would also continue to store small quantities of nitrogen and large quantities of fat, which indicates a marked disturbance in the intermediate metabolism. He also observed that there was a relatively uniform increase in the weight of the femurs and slow skeletal growth. The rate of gain was about 10 per cent of that of the controls. The uniformity of the increase indicated that it was probably not due to the presence of residual hormone during the first few days but was a basal growth level which could be maintained in the absence of pituitary hormones. That regeneration as well as growth is interfered with is shown by a failure of regenerative powers following hypophysectomy in the newt.<sup>39</sup>

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36. (a) Smith, P.: The Disabilities Caused by Hypophysectomy and Their Repair, *J. A. M. A.* **88**:158 (Jan. 15) 1927. (b) Smith, P. E.: Hypophysectomy and a Replacement Therapy in the Rat, *Am. J. Anat.* **45**:205, 1930. (c) Freud, J.; Levie, L. H., and Kroon, D. B.: Observation on Growth (Chondrotrophic) Hormone and Localization of its Point of Attack, *J. Endocrinol.* **1**:56, 1939.

37. (a) Reichert, F. L.: The Results of Replacement Therapy in an Hypophysectomized Puppy, *Endocrinology* **12**:451, 1928. (b) Dandy, W. E., and Reichert, F. L.: Studies on Experimental Hypophysectomy in Dogs, *Bull. Johns Hopkins Hosp.* **62**:122, 1938. (c) Crowe and others.<sup>25</sup> (d) Aschnan.<sup>26</sup>

38. Samuels, L. T.; Reinecke, R. M., and Bauman, K. L.: Growth and Metabolism of Young Hypophysectomized Rats Fed by Stomach Tube, *Endocrinology* **33**:87, 1943.

39. Richardson, D.: Thyroid and Pituitary Hormones in Relation to Regeneration, *J. Exper. Zool.* **100**:417, 1945.

Histologically certain changes are observed constantly after hypophysectomy.<sup>40</sup> In the epiphysial line the cells in the zone of proliferation are small, with pyknotic nuclei, and are reduced in number. The cartilage columns are regular but narrower, with an increased amount of matrix between them. The cells of the vesicular zone appear shrunk and the lacunas small, and there is a narrowing of this zone. The erosion zone is inactive. In the diaphysis the disappearance of the trabeculae is striking, which is explained only by an actual absorption of bone without an actual increase in the number of osteoclasts. The marrow shows a tremendous increase in fat content at the expense of the myeloid elements. As a result of these changes there is then, about twenty-five days after hypophysectomy, a reduction in the width of the epiphysial line. The progressive, severe atrophy of both the primary and secondary spongiosa may be seen by the seventh to the thirteenth day.<sup>41</sup>

Accompanying the changes in skeletal growth there are also gross and microscopic changes in other organs.<sup>42</sup> All organs are normal with the exception of the thyroid and adrenal glands and the gonads. Grossly there is atrophy of the adrenal cortex, but microscopically there is no deviation from the normal. The testes or ovaries are atrophied and show all signs of immaturity. There is little glandular tissue in the breasts of the animals. The changes in the thyroid are constant. There is pronounced atrophy, with smaller acini and a diminished amount of colloid.<sup>37b</sup>

The great reduction in the growth of the skeleton and musculature in the presence of available foodstuffs would favor the view that there is a reduction in the ability to synthesize structural elements following hypophysectomy, but the fact that wounds heal readily in hypophysectomized animals<sup>38</sup> indicates that the process is not completely inhibited. The slow increase in carcass nitrogen and the gradual growth of some organs further support the hypothesis that the removal of the pituitary gland eliminates a factor which catalyzes the growth process but which is not essential for it. It is possible that the synthesis of proteins is catalyzed by pituitary hormones.

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40. (a) Beck, H. M.; Simpson, M. E.; Marx, W., and Kibrick, E.: Bioassay of the Pituitary Growth Hormone, *Endocrinology* **32**:13, 1943. (b) Ray, R. D.; Evans, H. M., and Becks, H.: Effect of the Pituitary Growth Hormone on the Epiphyseal Disc of the Tibia of the Rat, *Am. J. Path.* **17**:509, 1941.

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42. Footnotes 27 and 36 *a*, *b*.

## HYPOPITUITARY STATES AND RELATIONSHIP TO HEREDITARY DWARFISM

Retardation of growth is seen in human beings as well as in experimental animals in association with hypopituitarism. Simmonds<sup>43</sup> in 1916 described a 9 year old girl who died of conditions simulating the emaciation of tuberculosis and who at autopsy was found to have a basophilic tumor of the hypophysis that had destroyed the remainder of the gland substance, but Erdheim<sup>44</sup> was the first to recognize the hypophysial origin of a dwarflike stunting of growth which may occur with the early destruction of the hypophysis—in his case a teratoma. The skeleton in such cases remains like that of a child with open epiphysal lines, with atrophy of the thyroid, gonads and adrenal glands. The characteristic delay in development of the ossification centers is the prominent feature, the epiphyses remaining open beyond the usual time. This growth defect, combined with delayed and subnormal sexual maturation, normal intelligence and normal mental faculties, is typical of the hypopituitary dwarf.<sup>45</sup>

The growth pattern of clinical hypopituitarism corresponds, then, to that seen in experimental animals in that there is a certain amount of growth at a basal level, which will occur in the presence of adequate foodstuffs.

Hereditary dwarfism appears as a mutation in the mouse. Since these dwarfs are entirely sterile, they can be produced only by heterozygous parents or occasionally from one that has received pituitary replacement therapy. There are no eosinophils in the anterior pituitary in the dwarfs. The dwarfism is essentially a retarded skeletal time curve, since they will continue to grow after normal mice have ceased to grow.<sup>46</sup> These animals are not true hereditary dwarfs, the term being reserved for dwarfs that are normal in every respect except for their size.

True hereditary dwarfism in the human being occurs but is not a true pathologic condition, for neither the skeleton nor other organs show evidence of abnormality or disease except for their small size. Puberty occurs at the normal age, and sex function is normal. Growth is slow and far below average, and this applies to the differential growth

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43. Simmonds, M.: Ueber Kachexie hypophysären Ursprungs, *Deutsche med. Wehnschr.* **42**:190, 1916.

44. Erdheim, J.: Pathologie der Hypophysengeschwulste, *Ergebn. d. allg. Path. u. path. Anat.* **21**(11):482, 1926.

45. (a) Gardiner-Hill, H.: Abnormalities of Growth and Development, *Brit. M. J.* **1**:1302, 1937. (b) Shelton, E. K.: The Clinical Aspects of Dwarfing, *Endocrinology* **30**:1000, 1942. (c) Grollman, A.: *Essentials of Endocrinology*, ed. 2, Philadelphia, J. B. Lippincott Company, 1947, p. 101.

46. Boettiger, E., and Osborn, C. M.: A Study of Natural Growth and Ossification in Hereditary Dwarf Mice, *Endocrinology* **22**:447, 1938.

of the skeleton as well. The racial form is typified by the pygmies of Central Africa and is essentially a hereditary characteristic and dependent on the genetic constitution.<sup>47</sup>

Although endocrine constitution is largely determined by heredity, work of experimental embryologists suggests that the endocrine influences are not the main cause of racial peculiarities. Harrison,<sup>48</sup> in experimental work on transplantation of limbs of salamanders, has shown that in the same endocrine environment limbs and other structures from two species of different sizes will maintain their own rate of growth and reach the ultimate size and form characteristic of the species. This work indicates that there is an inherited growth capacity which is influenced by, but not dependent on, the endocrine constitution of the individual.

EFFECT OF SUBSTITUTION THERAPY WITH EXTRACTS OF THE  
ANTERIOR HYPOPHYSIS ON NORMAL AND HYPOPITUITARY ANIMALS AND ON HUMAN BEINGS

After Evans' work,<sup>29</sup> in which alcoholic extracts of the anterior pituitary produced marked alterations of the growth pattern in experimental rats, a great deal of work has been done, some of which has led to conflicting conclusions. A pure substance from the anterior lobe of the pituitary which will produce an effect only on skeletal growth has not been chemically isolated and identified, and this partially accounts for so much divergence of opinion. A globular fraction has been separated from extracts of the anterior hypophysis which contains the growth-promoting principle.<sup>49</sup> From osmotic pressure determinations the molecular weight is 44,250, and experiments with electrophoresis show an isoelectric point at  $p_H$  6.85. The hormone is more stable in alkaline solution and can be destroyed by pepsin and trypsin.<sup>50</sup> The effect on the epiphysis of this substance when administered to hypophysectomized rats is so uniform that this reaction has been used for its bioassay.<sup>40a</sup> The initial effect on the epiphysial cartilage is predominantly chondrogenesis. Activation of osteogenesis follows later, after six to eight days, at which time the normal equilibrium between chondrogenesis and osteogenesis is established, with a return of the

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48. Harrison, R. G.: Heteroplastic Grafting in Embryology in *Harvey Lectures, 1933-1934*, Baltimore, Williams & Wilkins Company, 1935, p. 116.

49. Teel, H. M.: A Method for Purification of Extracts Containing the Growth Promoting Principle of the Anterior Hypophysis, *Science* **69**:405, 1929.

50. Li, C. H.; Evans, H. M., and Simpson, M. E.: Isolation and Properties of the Anterior Hypophyseal Growth Hormone, *J. Biol. Chem.* **159**:353, 1945.

youthful type of epiphysial cartilage.<sup>51</sup> This activation of osteogenic processes can be accomplished as long as one year or more after hypophysectomy in the rat,<sup>52</sup> and it can be accomplished when other known contaminating hormones are removed, as evidenced by the continued growth with no change in the atrophic thyroid, gonads or adrenal cortex.<sup>53</sup>

Replacement therapy using homeotransplants of the anterior pituitary in the rat restores the animals to normal, or nearly normal.<sup>36a, b</sup> Heterotransplants in puppies<sup>37a</sup> using the rabbit pituitary will stimulate the growth but not for a period sufficient for the animals to obtain normal size before closure of the epiphysial lines occurs.

Injection of anterior pituitary extract in normal growing rats causes a decided stimulation of endochondral ossification, with little disturbance of the equilibrium between the formation of cartilage and bone, and an overstimulation of normal periosteal bone growth.<sup>54</sup> This response is not changed by thyroparathyroidectomy.<sup>55</sup> In 6 month old rats which have reached a physiologic state of growth inactivity (the epiphyses do not close in the rat) there is growth response after the anterior lobe extracts are administered and histologic evidence of active growth in the epiphysial cartilage plates and in the adjacent spongiosa.<sup>56</sup> Similar stimulative effects are noted in the growing guinea pig and dog,<sup>57</sup>

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51. (a) Marx, W.; Simpson, M. E., and Evans, H. M.: Specificity of the Epiphyseal Cartilage Test for the Pituitary Growth Hormone, *Proc. Soc. Exper. Biol. & Med.* **55**:250, 1944. (b) Becks, H.; Simpson, M. E.; Marx, W.; Li, C. H., and Evans, H. M.: Antagonism of Pituitary Adrenocorticotrophic Hormone (ACTH) to Action of Growth Hormone on Osseous System of Hypophysectomized Rats, *Endocrinology* **34**:311, 1944. Freud and others.<sup>36c</sup> Ray and others.<sup>40b</sup>

52. Becks, H.; Simpson, M. E.; Evans, H. M.; Ray, R. D.; Li, C. H., and Asling, W.: Response to Pituitary Growth Hormone and Thyroxin of the Tibias of Hypophysectomized Rats after Long Post-Operative Intervals, *Anat. Rec.* **94**:631, 1946.

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54. Handelsman, M. B., and Gordon, E. F.: Growth and Bone Changes in Rats Injected with Anterior Pituitary Extract, *J. Pharmacol. & Exper. Therap.* **38**:349, 1930. Ray, R. D.; Evans, H. M., and Becks, H.: The Effect of Growth Hormone Injections on the Costochondral Junction of the Rat Rib, *Anat. Rec.* **82**:67, 1942. Ray and others.<sup>40b</sup>

55. Becks, H.; Kibrick, E. A., and Evans, H. M.: The Bone Histology of Adult Male Rats Thyro-Parathyroidectomized When One Month of Age, *J. Exper. Zool.* **89**:297, 1942.

56. Ross, E. S., and McLean, F. C.: The Influence of the Growth Promoting Hormone of the Anterior Lobe of the Pituitary upon Growth Activity in the Long Bones of the Rat, *Endocrinology* **27**:329, 1940.

57. Silberberg, M.: Effects of Extract of Cattle Anterior Pituitary Gland on Endochondral Ossification in Young Guinea Pigs, *Proc. Exper. Biol. & Med.* **32**:1423, 1935.

in which there is hypertrophy and hyperplasia of the growth cartilage, which is subsequently quickly calcified and replaced by bone. The epiphysial line, therefore, undergoes premature closure under the influence of the extract. Another instance of the acceleration of the tissue time curve by the administration of pituitary extracts is shown by the acceleration of the formation of cancellous bone occurring in the abdominal fascia around the urinary bladder transplants of young pigs.<sup>58</sup>

In dwarf mice, in which there is a hereditary absence of the eosinophilic cells in the anterior pituitary, with resultant retarded skeletal time curve, daily implantations of normal pituitaries will restore normal growth. Riddle and others<sup>59</sup> have been able to restore skeletal growth in these mice by using prolactin and thyrotropic hormones either separately or together, when there is a synergistic action. This has been the basis for their contention that the growth hormone is not an individual factor but that it is a summation of several stimulating actions through other endocrine glands.

Clinically the treatment of true pituitary dwarfism has been unsatisfactory apparently because there is no highly potent and purified preparation for clinical use.<sup>60</sup>

#### HYPERPITUITARISM

The strongest evidence in favor of a specific growth hormone being secreted by the hypophysis is the clinical occurrence of gigantism in the adolescent and of acromegaly in the adult in association with evidence of overactivity of the hypophysis. Experimentally a mild degree of gigantism in rats was produced by Evans and Long,<sup>29</sup> but this is not easily or consistently produced, and the degree of overgrowth is limited. Others<sup>61</sup> have produced a condition in dogs, by using anterior pituitary extract, simulating the acral enlargement observed in human acromegaly. Definite skeletal overgrowth with hyperostosis is seen in these animals at autopsy.

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58. Silberberg, M.; Atherton, H. R., and Copher, G. H.: Effects of Bovine Anterior Hypophyseal Extract on Urinary Bladder Transplants in Young Dogs, *Ann. Surg.* **120**:680, 1944.

59. Bates, R. W.; Loanes, T., and Riddle, O.: Evidence from Dwarf Mice Against the Individuality of Growth Hormone, *Proc. Soc. Exper. Biol. & Med.* **33**:446, 1935.

60. (a) Finkler, R. S.; Furst, N. J., and Klein, M.: Clinical and Roentgenological Study of the Effects of Hormonal Therapy on Bone Growth, *Radiology* **43**:346, 1944. (b) McCullagh, E. P., and Rossmiller, H. R.: Methyl Testosterone—Effect upon Body Weight and Growth, *J. Clin. Endocrinol.* **1**:507, 1941. (c) Grollman.<sup>45c</sup>

61. Putnam, T. J.; Benedict, E. B., and Teel, H. M.: Experimental Canine Acromegaly Produced by Injection of Anterior Lobe Pituitary Extract, *Arch. Surg.* **18**:1708 (April) 1929. Teel, H. M., and Cushing, H.: Studies in the Physiological Properties of the Growth-Promoting Extracts of the Anterior Hypophysis, *Endocrinology* **14**:157, 1930.

True pituitary gigantism is rare because the eosinophilic adenoma of the anterior pituitary usually occurs in adult life.<sup>47</sup> When it does occur, it usually starts at the time of puberty. Acromegaly is almost always associated with an eosinophilic adenoma or hyperplasia of the acidophilic cells of the anterior hypophysis. This was demonstrated in all but 2 of the 100 cases analyzed by Bailey and Davidoff<sup>62</sup> and is generally accepted to be a constant finding. In gigantism the increased growth is symmetric, but it is usually followed by the asymmetric growth characteristic of acromegaly when the major epiphyses close, producing an acromegalic giant.

Just as true hereditary dwarfism is not a pathologic condition, true hereditary gigantism is not a pathologic condition. Neither the skeleton nor other organs show any evidence of abnormality or disease except for their size. It is a hereditary characteristic and dependent on the chromosomal rather than the endocrine constitution.<sup>63</sup>

#### HYPOTHYROIDISM AND ATHYROIDISM

As noted earlier, a relationship between skeletal growth and the activity of the thyroid gland was noted early in the history of endocrinology. Experimentally, young rats,<sup>64</sup> dogs and cats,<sup>65</sup> rabbits,<sup>66</sup> frogs,<sup>67</sup> monkeys,<sup>68</sup> sheep and goats<sup>69</sup> show considerable retardation

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62. Bailey, P., and Davidoff, L. M.: Concerning the Microscopic Structure of the Hypophysis Cerebri in Acromegaly, *Am. J. Path.* **1**:185, 1925.

63. Gardiner-Hill.<sup>47</sup> Harrison.<sup>48</sup>

64. (a) Hammett, F. S.: The Effects of the Loss of the Thyroid and Parathyroid Glands at One Hundred Days of Age on the Growth in Body Length, Body Weight and Tail Length of Male and Female Albino Rats, *Am. J. Physiol.* **63**:218, 1922. (b) Salmon, T. N.: The Effect in the Growth Rate of Thyroparathyroidectomy in Newborn Rats and of the Subsequent Administration of Thyroid, Parathyroid and Anterior Hypophysis, *Endocrinology* **23**:446, 1938. (c) Becks, H.; Ray, R. D.; Simpson, M. E., and Evans, H. M.: Effect of Thyroxin and the Anterior Pituitary Growth Hormone on Endochondral Ossification, *Arch. Path.* **34**:334 (Aug.) 1942.

65. Dott, N. M., and Frazier, J.: The Influence of Experimental Pituitary and Thyroid Derangements upon the Developmental Growth of Bone, Abstract, communication to the Eleventh International Congress of Physiology, Edinburgh, 1923, p. 107.

66. Hunter, M. W., and Sawin, P. B.: The Effects of Thyroidectomy on the Skull of the Domestic Rabbit, *Am. J. Anat.* **71**:417, 1942.

67. Terry, G. S.: Effects of the Extirpation of the Thyroid Gland upon Ossification in *Rana Pipiens*, *J. Exper. Zool.* **24**:567, 1917-1918.

68. Fleischmann, W.; Shumacker, H. B., Jr.; Straus, W. L.: Influence of Age on the Effect of Thyroidectomy in the Rhesus Monkey, *Endocrinology* **32**:238, 1943.

69. Goldberg, S. A., and Simpson, S.: Osseous and Muscular Changes in Thyroidectomized Sheep, *Proc. Soc. Exper. Biol. & Med.* **23**:132, 1926.

of growth as one of the manifestations of thyroidectomy. Similarly, a delay in the unfolding of the osseous framework in children in association with a hypothyroid state is a constant finding.<sup>70</sup> In fact, in the absence of other pathologic changes, the skeletal development in childhood has been regarded as a reliable index of the metabolic speed.<sup>71</sup>

Experimentally the degree of growth retardation varies with the species and with the age at which the hypothyroidism occurs. There is notable retardation in the appearance and development of the ossification centers, and, in prolonged thyroid deficiency, certain degenerative changes are noted in the cartilaginous epiphyses.<sup>69</sup> The epiphysal cartilages remain wide and infantile in appearance,<sup>65</sup> and histologically they show a lesser degree of calcification than normal and the proportion of matrix to cartilage cells is greater. There are depressed osteoblastic activity, inadequate capillary erosion, thick cartilaginous trabeculae and a marked increase of fat in the marrow.<sup>72</sup> This histologic picture, then, is not too unlike that seen after hypophysectomy.

In hypothyroidic infantilism in children, dwarfism is pronounced if the onset is early in life. Skeletal proportions are those of an infant, the head being large for the body and the limbs shorter in proportion to the trunk, with a resultant disproportionate skeleton. The ossification centers appear late, and when they do appear, they develop slowly. In the epiphysal center there may be multiple irregular islets of calcification, which may enlarge and coalesce to form an irregular, spongy, fluffy mass similar to that seen in osteochondritis.<sup>73</sup> The histologic changes in the epiphysal plate are similar to those seen in experimental hypothyroidism.<sup>45a</sup> While the skeletal changes are not too different from those in pituitary dwarfism, the similarity ends there, as the mental retardation and physical appearance make the thyroid dwarf strikingly different from the pituitary dwarf. Hypothyroid dwarfs also show a much greater degree of osseous retardation than pituitary dwarfs of the same chronologic age.<sup>45b</sup>

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70. (a) Dorff, G. B.: Masked Hypothyroidism in Children, *J. Pediat.* **6**:789, 1935. (b) Shelton, E. K.; Lager, B. N., and Hoyt, E.: Cretinism, *Endocrinology* **27**:425, 1940. (c) Gardiner-Hill.<sup>45a</sup> (d) Shelton.<sup>45b</sup>

71. Shelton, E. K.: Osseous Development as an Index of Metabolic Speed, *Endocrinology* **17**:667, 1937.

72. Becks and others.<sup>64c</sup> Dott and Frazier.<sup>65</sup> Goldberg and Simpson.<sup>69</sup>

73. Lāwen, A.: Zur Kenntnis, der Wachstumsstörungen am Kretinenskelett, *Deutsche Ztschr. f. Chir.* **101**:454, 1909. Reilly, W. A.: Cretinoid Epiphysal Dysgenesis, *J. Pediat.* **11**:786, 1937. Wilkins, L.: Epiphysal Dysgenesis Associated with Hypothyroidism, *Am. J. Dis. Child.* **61**:13 (Jan.) 1941. Brailsford, J. F.: *The Radiology of Bones and Joints*, ed. 3, Baltimore, Williams & Wilkins Company, 1945, p. 134.



In addition to the skeletal changes following hypothyroidism, pronounced structural changes in the pituitary have been observed.<sup>74</sup> There is an increase in the size and weight of the gland, reduction in the number of acidophils and an increase in the number of basophils, many of which are distended with a hyaline material. The gonads and secondary sexual organs are small and atrophic. The parathyroids, thymus and adrenals are normal.<sup>75</sup>

Replacement therapy in cretinic dwarfs results in a constant response. The first year there is usually 600 to 900 per cent of the previous annual increment, in the second year there is 25 to 50 per cent of the previous annual increment and in the third year growth will proceed at about the normal rate, but the expected normal skeletal development for the individual will not be achieved.<sup>76</sup> There is no adequate explanation for the initial spurt of growth in these dwarfs when they are given thyroid therapy. A normal growth curve can be obtained experimentally by continued administration of thyroid after thyroidectomy,<sup>64b</sup> and the normal histologic picture in the pituitary is maintained or, if a previous deficiency existed, restored.<sup>74c</sup>

#### HYPERTHYROIDISM

Hyperfunction of the thyroid gland in young persons produces a striking increase in the rate of development and of growth of the skeletal system, with advancement in the apparent age of the ossification centers being a constant roentgenologic finding.<sup>77</sup> Beilby<sup>78</sup> reported a case in which the onset of hyperthyroidism occurred before 1 year of age. At the chronologic age of 4 the skeletal age was that of a 9 year old child. While there is definite stimulation in the rate of growth, it is not enhanced as much as the skeletal aging, so that the final total growth may be less than would be expected. Because of this, gigantism is not produced by hyperthyroidism.

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74. (a) Severinghaus, A. E.; Smelser, G. K., and Clark, H. M.: Anterior Pituitary Changes in Adult Male Rat Following Thyroidectomy, *Proc. Soc. Exper. Biol. & Med.* **31**:1127, 1934. (b) Liddell, H. S.: The Growth of the Head in Thyroidectomized Sheep, *Anat. Rec.* **30**:327, 1925. (c) Zeckwer, I. T.: Differences Between Castration Cells and Thyroidectomy Cells of the Pituitary of the Rat in Response to the Administration of Estrone and Thyroid Extract, *Am. J. Path.* **14**:773, 1938.

75. Moore, R. A.: *A Textbook of Pathology*, Baltimore, W. B. Saunders Company, 1944, p. 1059.

76. Shelton.<sup>45b</sup> Shelton and others.<sup>70b</sup>

77. Welti, H.: *Maladie de Basedow chez l'enfant*, Tr. Third Internat. Goiter Conf. & Am. A. Study Goiter, 1938, p. 101; cited by Black, J. B., and Webster, B.: Hyperthyroidism in Adolescent: Analysis of Eighteen Cases Under Eighteen Years of Age, *J. Clin. Endocrinology* **1**:861, 1941.

78. Beilby, G. E., and McClintock, J. C.: *Hyperthyroidism in Children*, New York State J. Med. **37**:563, 1937.

In mice <sup>79</sup> and rats, <sup>80</sup> experimental hyperthyroidism accelerates and intensifies the age changes of the skeleton. Thyroxin accelerates the conversion of the proliferating cartilage cells into cartilage cells of the hypertrophic type. It accelerates and increases the resorptive processes in the osseous tissues, leading to a complete epiphysiodiaphysial union at a premature age. Thyroid feeding in rats is followed by structural changes in the pituitary. The basophils are of maximum size and markedly increased in number. The acidophils are larger and stain more brilliantly <sup>81</sup>; however, no consistent changes are found in the anterior lobe of the pituitary in the human being in association with exophthalmic goiter. <sup>82</sup>

#### RELATIONSHIP OF THE THYROID AND THE PITUITARY

The interdependence of the pituitary gland and the thyroid gland for normal activity is exhibited by several different reactions. The atrophy of the thyroid in hypopituitary states and the hyperplasia in hyperpituitarism were discussed previously, as was the decreased number of eosinophilic cells in the anterior pituitary in hypothyroidism. Experimentally it was noted that there was hyperplasia of the eosinophilic cells in rats in hyperthyroidism, but this finding has not been apparent in human beings.

The thyroid response has been shown to be a result of the influence of the thyrotropic principle and not of the growth-promoting extracts, <sup>82b</sup> which exert their influence independently of the thyroid as demonstrated by the growth response to anterior pituitary extracts in thyroidectomized rats <sup>83</sup> and by the failure of growth in hypophysectomized animals treated with thyroid. <sup>84</sup> It has been suggested <sup>85</sup> that

79. Silberberg, M., and Silberberg, R.: Changes in the Skeletal Tissues of Mice Following the Administration of Thyroxin, *Growth* **4**:305, 1940.

80. Smith, E. E., and McLean, F. C.: Effect of Hyperthyroidism upon Growth and Chemical Composition of Bone, *Endocrinology* **23**:546, 1938. Becks and others. <sup>64c</sup>

81. Severinghaus, A. E.; Smelser, G. K., and Clark, H. M.: Anterior Pituitary Changes in Adult Male Rats Following Thyroxin Injections or Thyroid Feeding, *Proc. Exper. Biol. & Med.* **31**:1125, 1934.

82. (a) Wegelin, C.: L'hypophyse dans la maladie de Basedow, *Ann. D'anat. Path.*, **15**:703, 1938, cited by Grollman, A.: *Essentials of Endocrinology*, Philadelphia, J. B. Lippincott Company, 1947, p. 217. (b) Cope, C. L.: The Anterior Pituitary Lobe in Graves' Disease and in Myxoedema, *Quart. J. Med.* **7**:151, 1938.

83. Silberberg, M., and Silberberg, R.: Effect of Acid Extract of Cattle Anterior Pituitary on Bone Repair in Thyroidectomized Guinea Pigs, *Proc. Soc. Exper. Biol. & Med.* **34**:108, 1936.

84. (a) Evans, H. M.; Simpson, M. E.; Pencharz, R. I.: Relation Between the Growth Promoting Effects of the Pituitary and the Thyroid Hormone, *Endocrinology* **25**:175, 1939. (b) Smith. <sup>86a</sup>

85. Evans, H. M.: Clinical Manifestations of Dysfunction of the Anterior Pituitary, *J. A. M. A.* **104**:465 (Feb. 9) 1935.

thyroid dwarfism is directly caused by inadequate pituitary function secondary to thyroid subnormality. If so, then the restoration of growth could be accomplished by the administration of either thyroid or pituitary extracts. This has been partially accomplished experimentally in rats,<sup>84a</sup> but clinical use of pituitary extracts in persons with hypothyroidism has been disappointing<sup>80</sup> in that no significant response has been found. This may be due to the lack of potency of the extract, but more probably the action of the thyroid hormone on growth is a phase of its action on metabolism and is less specific and essentially different from that of the anterior pituitary.

It is true, however, that the two hormones have a synergistic action when administered to normal rats,<sup>84a</sup> to thyroidectomized rats,<sup>64c</sup> to hypophysectomized and thyroidectomized rats<sup>63</sup> or to hypophysectomized rats.<sup>52</sup>

From the evidence available, it would seem that the capacity for growth is more dependent on the action of the pituitary and the intensity of growth is more dependent on the action of the thyroid hormone.

#### HYPOGONADISM

The effects of castration and of hypogonadism from other causes on skeletal growth in animals and human beings may be observed in ordinary life. Castration is a common practice, and it is well known that in animals castrated during the growth period longer limbs develop and that in the eunuch the extremities are longer in comparison with the trunk. It is also readily seen that true gigantism does not occur, and hence it is apparent that the sex hormones are not fundamentally necessary for the cessation of skeletal growth but only influence it. With these indisputable facts at hand, it would seem necessary to determine only the manner and degree in which the gonads influence growth; however, conflicting reports have been published on the effects of castration on growth.<sup>87</sup> Experimentally, most workers report a depression of growth following castration. There is a delay in the development of the epiphysial cartilages, followed by a reduction in the rate of pro-

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86. Beard, E. E.: Cretinism, *J. Clin. Endocrinol.* **1**:293, 1941. Finkler and others.<sup>60a</sup> Shelton and others.<sup>70b</sup>

87. Pomerat, G. R., and Coe, R. C.: Bone Growth in the Long Term Castrate Albino Rat, *Endocrinology* **29**:1015, 1941. Rubinstein, H. S.; Abarbanel, A. R., and Kurland, A. A.: The Effect of Castration on Body Weight and Length of the Male Albino Rat, *Endocrinology* **25**:397, 1939. Tang, Y. Z.: Sex Difference in Growth in Gonadectomized Albino Rats, *Anat. Rec.* **80**:13, 1941. Silberberg, M., and Silberberg, R.: Effects of Ovariectomy and Long Continued Administration of APE of Cattle on Skeletal Tissues of Immature Guinea Pigs, *Am. J. Path.* **16**:505, 1940. Becks and others.<sup>52</sup>

lification at the epiphysis, which represents the direct cause of the temporary reduction in body length seen in castrated animals. The epiphyses, however, remain open beyond the normal time, accounting for the mild disproportionate gigantism seen, with the extremities unduly long in comparison to the trunk.

After castration there are rather constant cellular reactions in the hypophysis. In rats, there is a decrease in the size and number of the acidophils and an increase in the number and size of basophils, some of which become vacuolated and assume a "signet ring" appearance and are known as "castration cells."<sup>74c</sup> At the same time, there is an increase in the gland's content of gonadotropic principles, probably due to the absence of an "inhibitor" substance of the gonads.<sup>88</sup> This increase in gonadotropic substance is probably associated with the changes in the basophilic cells, the changes in the eosinophilic elements representing the depressed growth.

#### HYPERGONADISM

Hypergonadism in the human being is found either with precocious development of the gonads, secondary to adrenal cortical tumors,<sup>89</sup> with certain tumors of the testicles or ovaries or in association with hypothalamic lesions which presumably stimulate the production of gonadotropic substance in the anterior pituitary.<sup>90</sup>

In animals, however, experimental hypergonadism can be produced by the injection of sex hormones and related compounds.

Hypergonadism results in a marked acceleration of growth and speed of skeletal maturation. Rowlands<sup>91</sup> reported a 9 year old boy, normal at the age of 6, who had an interstitial cell tumor of the testis and who grew to 5 feet (152 cm.) in a period of three years. Krabbe,<sup>92</sup> studying roentgenograms of epiphyses of children with precocious puberty, found the skeletal age well in advance of the chronologic age and reported a case in which a girl was 54 inches (137 cm.) tall at 7 years of age. The final growth is less than would be normally expected, which indicates that skeletal maturation is advanced more rapidly than

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88. Best, C. H., and Taylor, M.: *The Physiological Basis of Medical Practice*, Baltimore, Williams & Wilkins Company, 1943, p. 1270.

89. Bergmann, B.: Sex Precocity and the Adrenogenital Syndrome, *J. Pediat.* **31**:142, 1947.

90. Gross, R. E.: Neoplasms Producing Endocrine Disturbances, *Am. J. Dis. Child.* **59**:579 (March) 1940.

91. Rowlands, R. P., and Nicholson, G. W.: Growth of the Left Testicle with Precocious Sexual and Bodily Development (Macro-Genito-Somia), *Guy's Hosp. Rep.* **99**:401, 1929.

92. Krabbe, K. H.: Early Synostosis of the Epiphyses with Dwarfism in Pubertas Precox, *Endocrinology* **3**:459, 1919.

skeletal growth. These studies also indicate that a sex hormone is related to the cessation of skeletal growth following puberty.

The use of estrogen, estrogenic substances and testosterone experimentally accelerates and intensifies the processes of skeletal aging and inhibits the proliferation of cartilage.<sup>93</sup> Daily injections of testosterone or estrogenic substances in castrated rats do not cause a change in the serum calcium or phosphorus, or in the fecal excretion of these elements,<sup>94</sup> or of the blood alkaline phosphatase.

With advancing age the following epiphyseal changes occur. There is a decrease in proliferation of cartilage cells and a decrease in the conversion of resting cartilage cells to hypertrophic cartilage cells. There is an increase in the amount of chondromucoid substance and an increase in sclerosis, hyalinization and calcification of the cartilaginous matrix. There is a continuous absorption and solution of the newly formed metaphyseal bone and finally of the nonproliferating epiphyseal disk, leading to epiphyseodiaphyseal union.<sup>95c</sup>

Injection of testosterone propionate in mice<sup>95</sup> and rats<sup>96</sup> promoted the aging of the epiphyseal cartilages by inhibiting proliferative processes and promoting degeneration, hyalinization, sclerosis and calcification in the cartilage except when only small doses were administered,<sup>97</sup> in which instance significant stimulation of growth was noted without significant advance in skeletal age. In castrated mice only small doses are required to restore development of growth and development of the epiphyseal cartilage,<sup>95a</sup> and hence this state probably more nearly approximates the normal. In rats the hypophyseal changes following castration

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93. (a) Silberberg, M., and Silberberg, R.: Response of Cartilage and Bone of Growing Mice to Testosterone Propionate, *Arch. Path.* **32**:85 (July) 1941; (b) Further Investigations Concerning the Influence of Estrogen on Skeletal Tissues, *Am. J. Anat.* **69**:295, 1941; (c) Effects of Hormones on the Skeleton of Mice, Guinea Pigs and Rats, *Endocrinology* **29**:475, 1941.

94. Buchwald, K. W., and Hudson, L.: The Biochemical Effects of Injections of Sex Hormones into Castrated Rats, *Endocrinology* **37**:301, 1945.

95. (a) Silberberg, M., and Silberberg, R.: Further Investigations on the Effect of the Male Sex Hormone on Endochondral Ossification, *Anat. Rec.* **95**:97, 1946; (b) footnote <sup>93a</sup>.

96. Rubinstein, H. S., and Solomon, M. L.: The Growth Depressing Effect of Large Doses of Testosterone Propionate in the Castrate Albino Rat, *Endocrinology* **28**:112, 1941.

97. Rubinstein, H. S.: Growth-Stimulating Effect of Testosterone Propionate, *Proc. Soc. Exper. Biol. & Med.* **44**:442, 1940. Rubinstein, H. S., and Solomon, M. L.: The Growth Stimulating Effect of Small Doses of Testosterone Propionate in the Castrate Albino Rat, *Endocrinology* **28**:229, 1941.

can be prevented by administration of testosterone.<sup>98</sup> Some workers<sup>99</sup> have failed to demonstrate any effect on skeletal growth by the use of testosterone, but for the most part these findings are accepted.

The use of testosterone as therapy for persons with hypogonadism has met with some success. There is a definite stimulation in the growth rate,<sup>100</sup> and if large doses are administered, significant advancement of the skeletal age over the chronologic age can be accomplished.<sup>101</sup> Weight cannot be used as a guide of growth because steroids, particularly those of the adrenal cortex, cause increase in weight for a while, owing to retention of sodium chloride and water.<sup>60b</sup>

As previously stated, injections of estrogen also accelerate skeletal aging in growing animals and when used over long periods, will cause significant retardation of growth in rats,<sup>102</sup> mice and guinea pigs.<sup>93b</sup> It inhibits the proliferation of cartilage and induces sclerosis of the cartilaginous matrix. On the other hand, estrogen inhibits processes of differentiation in the epiphyseal cartilage and counteracts the solution processes which normally lead to the removal of the subepiphyseal trabeculae and initiate epiphyseodiaphyseal union. At the same time, there is a definite osteosclerosis by endosteal appositional growth.<sup>103</sup> Since this does not reflect longitudinal growth, it is probably an attempt

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98. Wolfe, J. M., and Hamilton, J. B.: Response of Anterior Pituitary of Immature Castrated Rat to Testosterone and Related Compounds, *Proc. Soc. Exper. Biol. & Med.* **36**:307, 1937.

99. McEuen, C. S.; Selye, H., and Collip, J. B.: Effect of Testosterone on Somatic Growth, *Proc. Soc. Exper. Biol. & Med.* **36**:390, 1937. Turner, H. H.; Lachmann, E., and Hellbaum, A. A.: Effect of Testosterone Propionate on Bone Growth and Skeletal Maturation of Normal and Castrated Male Rats, *Endocrinology* **29**:425, 1941.

100. Webster, B., and Hoskins, W.: Influence of Androgen Therapy on Growth Rate of Hypogonadal Adolescent Boys, *Proc. Soc. Exper. Biol. & Med.* **45**:72, 1940.

101. McCullagh, E. P., and McGurl, F. J.: The Effect of Testosterone Propionate on Epiphyseal Closure, Sodium and Chloride Balance and a Sperm Count, *Endocrinology* **26**:377, 1940.

102. (a) Koenig, V. L.; Gassner, F. X., and Gustavson, R. G.: Effect of Estrone and Diethylstilbestrol on Growth Rate of Rats and on Iodine Content of Thyroid, *Am. J. Physiol.* **144**:363, 1945. (b) Gaarenstroom, J. H., and Levie, L. H.: Disturbance of Growth by Diethylstilbestrol and Oestrone, *J. Endocrinol.* **1**:420, 1939. (c) Spencer, J.; Gustavson, R. G., and d'Amour, F. E.: Effect of Estrin Injections on the Growth Curve of Young Rats, *Proc. Soc. Exper. Biol. & Med.* **28**:500, 1931. Talbot, N. B.: The Effect of Estrogen on the Skeletal Age of Immature Rats, *Endocrinology* **25**:325, 1939.

103. Sutro, C. J.: Effects of Subcutaneous Injection of Estrogen upon Skeleton in Immature Mice, *Proc. Soc. Exper. Biol. & Med.* **44**:151, 1940. Bauer, W., and Rub, J. C.: Studies of Calcium and Phosphorus Metabolism: XVI. The Influence of the Pituitary Gland, *J. Clin. Investigation* **20**:295, 1940.

to store calcium, so it is compatible that there would be stimulation of endosteal appositional growth with resultant osteosclerosis and yet be decreased epiphysial and periosteal bone growth.

In addition to these effects, estrogen injected produces effects on other endocrine glands. There is hypertrophy of the adrenal cortex and of the pituitary.<sup>104</sup> In the latter there is degranulation of many or all of the basophils, which indicates that these cells are the source of gonadotropic hormone, and if large doses are used there is also degranulation of the acidophilic elements corresponding with the decreased growth.<sup>105</sup>

Synthetic estrogens will produce the same effects on growth as natural estrogens,<sup>106</sup> the only difference being that administration of growth hormone does not counteract the action of synthetic estrogen.<sup>102b</sup>

#### ACTION AND RELATIONSHIP OF SEX HORMONES TO THE GROWTH HORMONE

Estrogen and growth hormone both accelerate skeletal aging in growing animals, but they accomplish this effect in different ways. The pituitary growth principle stimulates growth and hastens epiphyseodiaphysial union by inducing premature regression and resorption of the epiphysial cartilage; estrogen, on the other hand, inhibits growth and resorption, thus delaying epiphysiodiaphysial union. The skeletal effects of estrogen can be modified by the administration of growth hormone; the two hormones oppose each other in their action on the growth of cartilage, but they cooperate in accelerating the age changes in the cartilage and in the overproduction of bone growth hormone by stimulating osteoblastic bone formation and estrogen by promoting hyalinization of the marrow and by inhibiting the resorption of bone. The two hormones thus do not neutralize each other, but each tends to exert its own effect on the receptor tissue.<sup>107</sup> The effects of estrogen are direct and not mediated by the action of the anterior lobe of the hypophysis. The hypophysial changes thus observed in hypergonadism and hypogonadism are secondary manifestations.

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104. Korenchevsky, V., and Dennison, M.: Effect of Oestrone on Normal and Castrated Male Rats, *Biochem. J.* **28**:1474, 1934.

105. Wolfe, J. M., and Chadwich, C. S.: Quantitative Studies on the Structural Changes Induced in the Anterior Hypophysis by Injections of Oestrin, *Endocrinology* **20**:503, 1936. Wolfe and Hamilton.<sup>98</sup>

106. Noble, R. L.: Effect of Synthetic Oestrogenic Substance on the Body Growth and Endocrine Organs of the Rat, *Lancet* **2**:192, 1938. Koenig and others.<sup>102a</sup>

107. Silberberg, M., and Silberberg, R.: Combined Effects of an Estrogen and an APE on the Skeleton of the Growing Mouse, *Arch. Path.* **39**:381 (April) 1945.

Since the two hormones modify each other's effect to some extent, clinical use has been made of them. The use of ovarian extracts and testosterone has been moderately successful in arresting potential gigantism.<sup>108</sup>

#### RELATIONSHIP OF THE ADRENAL CORTEX TO BONE GROWTH

The relationship of the adrenal cortex hormone<sup>109</sup> to bone growth is less understood than that of the other endocrine substances. In adrenalectomized rats atrophy of the bone similar to that seen after hypophysectomy develops in five to eight days, which has led some<sup>41</sup> to believe that the organ is as essential for continued epiphysial growth as the pituitary and that both disturbances might have a common origin in the cessation of function of the adrenal cortex, since atrophy of the adrenal cortex is an inevitable sequence of hypophysectomy; however, these changes can be prevented in adrenalectomized animals by the administration of sodium chloride.<sup>110</sup>

By the administration of adrenal cortex hormone, crystalline derivatives of the hormone<sup>111</sup> or the adrenocorticotrophic principle of the pituitary to normal rats<sup>112</sup> and to castrated rats,<sup>113</sup> almost complete inhibition of somatic growth can be obtained. There is a retardation in both chondrogenesis and osteogenesis, but the reduction in the width of the epiphysial cartilage is not so extreme as that following hypophysectomy. Also, in hypophysectomized animals osteogenesis ceases, whereas in rats treated with adrenocorticotrophic hormone it continues

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108. Currier, F. P.; Frantz, C. H., and Vander Meer, R.: Reduction of Growth Rate in Gigantism Treated with Testosterone Propionate, *J. A. M. A.* **117**:515 (Aug. 16) 1941. Fancher, J. K.: Some Observations on Anterior Lobe Hyperpituitarism, *Endocrinology* **16**:611, 1932. Goldzieher, M.: Growth and Sex Hormones, *J. Clin. Endocrinol.* **1**:924, 1941.

109. Hartman, F. A., and Thorn, G. W.: A Biological Method for the Assay of Cortin, *Proc. Soc. Exper. Biol. & Med.* **28**:94, 1930. Hartman, F. A.; Brownell, K. A.; Hartman, W. E.; Dean, G. A., and MacArthur, C. C.: The Hormone of the Adrenal Cortex, *Am. J. Physiol.* **86**:353, 1928.

110. Simpson, M. E.; Marx, W.; Becks, H., and Evans, H. M.: Response of Adrenalectomized Hypophysectomized Rats to the Pituitary Growth Hormone, *Endocrinology* **35**:234, 1944.

111. Wells, B. B., and Kendall, E. C.: The Influence of Corticosterone and C17 Hydroxydehydrocorticosterone (Compound E) on Somatic Growth, *Proc. Mayo Clin., Staff Meet.* **15**:324, 1940.

112. Ingle, D. J.; Higgins, G. M., and Kendall, E. C.: Atrophy of the Adrenal Cortex in the Rat Produced by Administration of Large Amounts of Cortin, *Anat. Rec.* **71**:363, 1938.

113. Moon, H. D.: Inhibition of Somatic Growth in Castrate Rats with Pituitary Extracts, *Proc. Soc. Exper. Biol. & Med.* **37**:34, 1937.



at a reduced rate.<sup>114</sup> In hypophysectomized animals, the stimulating effect of the administration of growth hormone can be almost completely nullified by the simultaneous use of adrenocorticotrophic hormone.<sup>115</sup> If the animal is adrenalectomized, the adrenocorticotrophic hormone has no effect, as would be expected.<sup>116</sup> Adrenocorticotrophic hormone has no significant effect when administered alone to hypophysectomized animals.<sup>51a</sup> Animals which are both adrenalectomized and hypophysectomized show no more sensitivity to growth hormone when sodium chloride is given than do hypophysectomized animals.<sup>117</sup>

Clinically, excess secretion of the adrenals due to hyperplasia or neoplasm produces a marked advancement in growth and in skeletal age, but the advancement in skeletal age is greater in proportion than the spurt in growth.<sup>118</sup> Advancements of skeletal age from two to four years is not uncommon. There is an appreciable increase of androgens in the urine. While normally the steroids produced by the adrenal cortex are not androgenic, under pathologic influences androgenic steroids are produced.<sup>89</sup>

Usually the adrenal cortex probably has no relation to bone growth except as it is necessary for normal metabolism, but, in cases of tumor and other conditions producing hyperfunction certain steroids are excreted which produce the same effect as the sex hormones.

#### INDUCTION OF BONE GROWTH

From the evidence available, it is apparent that the thyroid, the gonads and the pituitary gland are intimately related to bone growth and to each other but that their function is more closely related to general tissue metabolism. Therefore, the question of their specificity is still debatable. The evidence indicates that their action is not specific but that their presence is essential for normal osseous growth. The decisive factor appears to be the "growth competence" of the tissue while the hormones act as growth organizers, the pituitary

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114. Becks, H.; Simpson, M. E.; Li, C. H., and Evans, H. M.: Effects of Adrenocorticotrophic Hormone (ACTH) on the Osseous System in Normal Rats, *Endocrinology* **34**:305, 1944.

115. Marx, W.; Simpson, M. E.; Li, C. H., and Evans, H. M.: Antagonism of Pituitary Adrenocorticotrophic Hormone to Growth Hormone in Hypophysectomized Rats, *Endocrinology* **33**:102, 1943. Becks and others.<sup>51b</sup>

116. Evans, H. M.; Simpson, M. E., and Li, C. H.: Inhibiting Effect of Adrenocorticotrophic Hormone on the Growth of Male Rats, *Endocrinology* **33**:237, 1943. Becks and others.<sup>114</sup>

117. Simpson, M. E.; Marx, W.; Becks, H., and Evans, H. M.: Effect of Testosterone Propionate on the Body Weight and Skeletal System of Hypophysectomized Rats, *Endocrinology* **35**:309, 1944.

118. Kennedy, R. L. J.: Precocious Skeletal Development, *J. A. M. A.* **127**:580 (March 10) 1945. Shelton.<sup>46b</sup> Gross.<sup>90</sup>

occupying the highest position. Furthermore, these hormones may act through an intermediary substance. Levander,<sup>119</sup> Lacroix<sup>120</sup> and Bertelsen<sup>121</sup> have been able to prepare an alcoholic extract of bone the fatty acid fraction of which when injected into muscular tissue produces cartilage and bone. Osteogenesis appears to occur by metaplasia of the surrounding connective tissue, the extract acting as a growth inductor. Blum,<sup>122</sup> in preparing phosphatase from long bones, found that the extract would produce ectopic bone when injected into muscles. Whether any relationship exists between these osteogenic substances and the hormones affecting bone growth remains to be seen.

#### SUMMARY

The longitudinal growth of long bones is primarily dependent on an inherited growth capacity and secondarily dependent on the endocrine constitution of the individual.

The secretions of the anterior lobe of the pituitary, the thyroid and the gonads are environmental factors in normal growth, and the secretions of the adrenal cortex may be under certain pathologic stimuli; of these, the anterior lobe of the pituitary occupies the highest order of the endocrine system.

The secretions of the anterior lobe of the pituitary, of the thyroid and of the gonads all accelerate and intensify the process of skeletal aging but accomplish this by each exerting its own effect on the receptor tissue.

These three organs are dependent on each other for their normal function.

A specific factor of the anterior pituitary is responsible for the maintenance of normal growth; however, a basal level of growth can be accomplished in its absence.

Thyroxin, by its action on metabolism, is primarily concerned with the intensity of growth.

Androgenic and estrogenic substances aid in the cessation of normal growth but are not essential for its occurrence.

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119. Levander, G.: A Study of Bone Regeneration, *Surg., Gynec. & Obst.* **67**:705, 1938. Levander, G.: Tissue Induction, *Nature, London* **155**:148, 1945. Levander, G.: Alcohol-Soluble Osteogenetic Substance from Bone Marrow, *Nature, London* **157**:587, 1946.

120. Lacroix, P.: Recent Investigations on the Growth of Bone, *Nature, London* **156**:576, 1945; On the Origin of the Diaphysis, *Anat. Rec.* **92**:435, 1945; Organizers and the Growth of Bone, *J. Bone & Joint Surg.* **29**:292, 1947.

121. Bertelsen, A.: Experimental Investigations into Post-Foetal Osteogenesis, *Acta. orthop. Scandinav.* **15**:139, 1944.

122. Blum, G.: Phosphatase and the Repair of Fractures, *Lancet* **2**:75, 1944.

## LIGATION OF THE VENA CAVA IN EXTENDING THROMBOPHLEBITIS

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THE TREATMENT of venous thrombosis has been revolutionized in the past two decades by the use of anticoagulant drugs (heparin sodium and dicumarol®) and by ligation of the involved veins (usually the femoral vein). Ligation of the inferior vena cava has been carried out infrequently. It is evident that in the past few years interest in, and a study of, this formerly rare procedure have been greatly accelerated. Doubtless, the motivating force behind this increased interest is the usefulness of ligation as an additional weapon in our armamentarium to forestall the sudden catastrophe of embolic disease. The use of this measure is not advocated as a replacement for anticoagulant therapy or for ligation of the femoral vein, but rather as an additional method for use when these procedures may be inadequate; we feel that ligation of the vena cava is indicated much more frequently than it is used. After a careful review of the available literature and after general consideration, we question whether it should not replace ligation of the iliac veins, especially the left one.

We wish to describe a group of symptoms and signs which we have not found described elsewhere and which we believe indicate involvement of the lumbar veins or the collateral veins by the spread of thrombophlebitis. These manifestations include pain and tenderness in the lumbar region and the loin and hyperesthesia in the distribution of the lumbar nerves. We believe ligation of the vena cava is indicated when these factors are present, as in the cases described.

### REPORT OF CASES

CASE 1.—A white youth of 17 was admitted to an Army and Navy general hospital on Sept. 3, 1946 with severe acute anterior poliomyelitis. Because of respiratory involvement he was immediately placed in a respirator, in which he remained for thirteen days; by the fifteenth day the respirator was no longer necessary. The involvement of the legs remained massive and was associated with severe muscular pains. On the twenty-fourth day after admission he first complained of pain in the right lower quadrant of the abdomen and in the right

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inguinal region. The temperature was 99 F., and the pulse rate was elevated to 96 beats per minute. Moderate tenderness was present in the right lower quadrant of the abdomen and in the right inguinal region; a greater degree of tenderness was noted over the femoral vessels. There was definite swelling of the right lower extremity. The leukocyte count was 15,700 per cubic millimeter, with a moderate shift to the left. A paravertebral block was performed on the right side, and therapy with heparin sodium and dicumarol® was begun.

On the following day, the patient was seen for the first time by the members of the surgery section; he then complained of increased pain in the thigh, the groin, and the right lower quadrant of the abdomen, and he had become nauseated.



Legs of the patient in case 1 ten months after operation. The patient had been on his feet, wearing long leg braces, for approximately one hour and had been sitting up with his legs dependent for approximately one-half hour before the photograph was taken.

Pronounced tenderness was present in the femoral and right inguinal regions and in the right lower quadrant of the abdomen, and the tenderness had extended into the right flank. The patient also was beginning to complain of some pain in the flank. There was hyperesthesia in the dermatomes supplied by the first to the fourth lumbar spinal nerves. Rectal tenderness was present, mostly on the right side. The diagnosis of thrombophlebitis seemed certain, and it was believed that there was extension into the right iliac vein. Dicumarol® therapy was continued. Findings on the second day after the onset of the pain were unchanged except

for increased pain and tenderness in the loin and beginning pain and tenderness in the left inguinal region. However, on the third day after onset the patient had a sudden severe pain in the right side of the chest accompanied with dyspnea, and he coughed up small amounts of blood-stained sputum. Rales were heard in the base of the right lung. As it seemed certain that he had had a pulmonary embolus, operation was carried out. Procaine hydrochloride (novocain®) was used for local anesthesia. A transperitoneal approach through a right transverse incision spared the inferior epigastric vessels. The right iliac vein was found to be occluded, the clot extending to the bifurcation and just into the left iliac vein, as well as into the vena cava. There was a moderate inflammatory reaction, with edema throughout the area involved, extending around the vena cava to a distance of about 1.5 cm. above the bifurcation. The peritoneum was incised over the vena cava, the vessel freed and a curved clamp passed around it; the clamp was then withdrawn with an umbilical tape, which was tied down firmly. Closure was carried out with silk. The postoperative course was uneventful except for distention, which was controlled without great difficulty. The swelling

TABLE 1.—*Circumference of Legs Before and After Ligation of the Vena Cava in Two Cases*

	Days Before Operation			Days After Operation												
	3	2	1	0	1	2	3	4	5	6	7	8	9	10	11	12
Case 1																
Right leg....	18.5*	20	20	20	20.2	20.5	20	18.7	19	18.7	18.6	18.5	....	18.25	....	18†
Left leg.....	17.0	17.5	17.5	17.5	17.5	17.2	16.7	16.5	16.5	16.9	16.6	16.1	....	16	....	16
Case 2																
Right leg....	....	17.0	17.0	17.5	19	19.5	20	20	20	19	18.7	18.5	18.5	17.8	17.5	17.2‡
Left leg.....	....	17.3	19.0	20	21	22	22	21.5	21	20.5	20	19	19.2	18.5	18	17.7

\* All measurements are given in inches.

† Measurements were next taken three months after operation, at which time both legs were 15.5 inches in circumference.

‡ The size of the genitalia had also returned to normal at this time.

of the legs increased only slightly after the operation and then slowly decreased, as shown in table 1. Despite the extremely poor muscular function necessitating his wearing braces, the patient showed no observable dependent edema, as indicated in the photograph. A roentgenoscopic examination with iodopyracet injection (diodrast®), made five months after the operation, showed no evidence of obstruction.

CASE 2.—A white man of 26 sustained a fracture of the twelfth dorsal vertebra with resultant complete paraplegia on Oct. 12, 1946 and was admitted directly to the hospital. On the eighth day after admission, swelling of the left ankle developed, thought to be due to a phlebothrombosis. By the next day, the swelling had extended up through the calf into the thigh. A course of heparin sodium and dicumarol® was begun. Later that day the patient began to complain of lower abdominal pain, and a general consultation concerning operation was held. At that time, there was pronounced edema of the left lower extremity, moderate edema of the scrotum and questionable swelling of the right lower extremity, established by measurement (table 2). There was tenderness in the lower part of the abdomen, especially in the left lower quadrant, and also in the left loin, where it was associated with some muscular spasm. The rectal examination showed tenderness on the left side. The temperature was 99 F., the pulse rate 100 beats

TABLE 2.—Cases of Ligation of the Inferior Vena Cava Reported in the Literature

Observer	No. of Cases	No. of Post-operative Deaths	Indication for Ligation	Date
Kocher, cited by Pfaff <sup>27</sup> and Northway and Burton <sup>23</sup>	1	1	Accidental	1883
Bilroth, cited by Pfaff, <sup>27</sup> Northway and Burton, <sup>23</sup> and Kern and Berman <sup>10</sup>	1	1	Hemorrhage from operative tear of vena cava	1885
Bottini, E.: Clin. chir. 12: 529, 1893	1	0	Hemorrhage from operative tear	1893
Héresco, P.: Proc. A. franç. d'urol. S: 777, 1905; cited by Miller <sup>12</sup> and Homans, J.: New England J. Med. 211: 993, 1934	1	0	Hemorrhage from operative tear	Before 1905
Albarran, cited by Kern and Berman <sup>10</sup>	1	0	Hemorrhage from operative tear	Before 1905
Houzel, G.: Rev. de chir. 27: 455, 1903	1	0	Hemorrhage from operative tear	1903
Hartman, H.: Bull. et mém. de la Soc. nat. de chir. 20: 57, 1904	1	0	Hemorrhage from operative tear	1904
Trendelenburg, F.: J. A. M. A. 47: 81 (July 14) 1906; also cited by Moses <sup>8</sup> and Miller <sup>12</sup>	3	2	Pelvic thrombophlebitis	1904 1906
Kohts, K.: Deutsche med. Wehnschr. 37: 666, 1911; also cited by Kern and Berman <sup>10</sup>	1	0	Hemorrhage from operative tear	1911
Bejan, I., and Cohn, M.: Rev. de chir. 43: 302, 1911	1	0	Hemorrhage from operative tear	1911
Fromme, cited by Miller <sup>12</sup> and Ochsner, A., and DeBaakey, M.: New England J. Med. 255: 207, 1941	1	1	External thrombosis of the iliac vein	Before 1925
Pfaff <sup>27</sup> .....	1	0	Hemorrhage from operative tear	1926
Patel, J.: Lyon chir. 24: 669, 1927	1	0	Hemorrhage from operative tear	1927
Dannheisser, F.: Zentralbl. f. Chir. 54: 2696, 1927	1	0	Hemorrhage from operative tear	1927
Schroeder, R.: Deutsche med. Wehnschr. 53: 903, 1927	1	0	Desired removal of thrombus in the inferior vena cava	1943
Atlas, L. N.: Ohio State M. J. 39: 917, 1943	1	0	Thrombophlebitis extending into the vena cava	1943
Collins, Jones and Nelson <sup>17</sup> .....	8	1	Pelvic thrombophlebitis	1943
Collins, Jones and Nelson, cited by Ochsner <sup>18</sup>	12	0	Pelvic thrombophlebitis	1945
Ochsner and DeBaakey <sup>1</sup> .....	3	0	Pelvic thrombophlebitis	1944
Kern and Berman <sup>10</sup> .....	1	0	Septic embolism associated with thrombophlebitis	1945
Burton and Collier <sup>21</sup> .....	7	0	Long-standing edema and phlebitis of legs, with and without ulceration	1945
Gaston and Folsom <sup>20</sup> .....	2	0	Thrombophlebitis with multiple emboli (1); continued pulmonary infarction after ligation of both femoral veins	1945
O'Neil <sup>22</sup> .....	8	0	Ascending thrombophlebitis (5); pulmonary embolism, source unknown (3)	1945
Northway and Burton <sup>23</sup> .....	10	0	Multiple pulmonary emboli (3); chronic edema of the leg without ulceration (4); chronic edema of the leg with ulceration (2); epigastric pain associated with phlebothrombosis (1)	1945
Kidd, H. A.: Brit. Surg. 73: 606, 1947	1	0	Injury to inferior vena cava by a bomb splinter	1945

TABLE 2.—*Cases of Ligation of the Inferior Vena Cava Reported in the Literature—Continued*

Observer	No. of Cases	No. of Post-operative Deaths	Indication for Ligation	Date
Veal and Hussey <sup>20</sup> .....	6	0	Bilateral thrombosis and emboli of the iliac vein (4); extension of inflammation from the left common iliac vein to the vena cava with embolism (2)	1945
Moses <sup>8</sup> . . . . .	21	*	(Includes both groups described at left) Recurrent emboli after bilateral ligation of the femoral vein (2); thrombosis of pelvic veins and infarction (2); pulmonary emboli associated with venous clot, fixed to the wall of the femoral vein and extending into the iliac vein (17); venous clot adherent to the femoral vein and extending into the iliac vein without emboli (11); phlebitis of the prostatic veins associated with emboli (11); pulmonary embolism associated with venous occlusion of lower vessels (usually treated by ligation of the femoral vein alone, but contraindicated in these cases by disease in the groin (2))	1946
Fraser, R. W.: Bull. U. S. Army M. Dept 5:357, 1946	1	0	Hemorrhage from the inferior vena cava secondary to shrapnel wound	1945
Thebout, B. R., and Ward, C. S.: Surg., Obst. & Gynec. 84:385, 1947	36	4	Thromboembolism	April 1947
Shafiroff, B. G. P.: Am. J. Surg. 73:621, 1947	1	0	Bilateral thrombophlebitis with embolism	May 1947
Kirk, G. D.: Am. J. Surg. 73:606, 1947	1	1	Extensive septic thrombophlebitis	May 1947

\* Reported 6 deaths in 21 ligations of the vena cava and 15 ligations of the common iliac vein.

per minute and the leukocyte count 13,700 per cubic millimeter. The dicumarol® therapy was discontinued, and vitamin K was given. An operation was performed under local anesthesia, as outlined in case 1, except for the use of a left transverse incision. The patient had increased edema, especially of the scrotum, for the first few days after the operation, but it rapidly subsided; by the twentieth day the size of the legs had returned practically to normal. The patient was transferred to another hospital two months after the operation, and other studies have not been possible.

#### COMMENT

No discussion of surgical treatment of thrombophlebitis or phlebothrombosis of the lower extremity of the pelvic veins would be complete without mention of the importance of prophylaxis against this serious condition. It is our feeling and apparently that of many writers (Ochsner and DeBakey,<sup>1</sup> Potts and Smith,<sup>2</sup> Hunter and others<sup>3</sup> and

1. Ochsner, A., and DeBakey, M.: Thrombophlebitis and Phlebothrombosis, in Lewis, D.: *Practise of Surgery*, Hagerstown, Md, W. F. Prior Company, Inc., vol. 12, chap. 5-B.

2. Potts, W. J., and Smith, S.: Pulmonary Embolism. An Experimental Study of Variations in the Volume of Blood Flow in the Inferior Vena Cava of the Dog, *Arch. Surg.* 42:661 (April) 1941.

3. Hunter, W. D.; Krygier, J. J.; Kennedy, J. C., and Sneedon, V. D.: Etiology and Prevention of Thrombosis of the Deep Leg Veins, *Surgery* 17:178, 1945.

Dock<sup>4</sup>) that adequate prophylaxis would prevent most occurrences of this condition, with its severe and often fatal complications. Furthermore, we believe that thrombosis in our surgical cases occurred only when patients were uncooperative in their routine or when some one of the necessary conditions to be described had not been carefully provided. Certainly, the 2 patients whose cases are reported did not have adequate prophylactic treatment.

Adequate prophylaxis includes the following: (1) preoperative preparation, with restoration of the body fluids and the circulation to normal; (2) careful placement of the patient on the table to prevent blocking of the venous return; (3) care in the operative technic, including atraumatic surgery, with the use of fine suture material and the avoidance of mass ligatures, the avoidance of damage to tissues and the prevention of shock, and (4) postoperative care, including an adequate, steady intake of fluids (to maintain venous filling) and continued postoperative exercises, commencing as soon as reaction has occurred. We believe that complete motion of both arms and both legs and deep breathing, performed at least twenty times every hour, is necessary. We feel that if such a regimen is carefully carried out thrombosis will be extremely rare and the occurrence of pulmonary emboli even less common. Other measures which have been advocated are use of the Trendelenburg position after the operation, and early ambulation. These factors have been stressed by Ochsner and DeBakey,<sup>1</sup> Frykholm,<sup>5</sup> Potts and Smith,<sup>2</sup> Hunter and others<sup>3</sup> and Dock.<sup>4</sup>

Early ambulation is used regularly in our cases, but we feel that its use does not decrease the necessity for the foregoing measures. It is our opinion that the few instances of thrombosis which we have observed occurred when the patients were uncooperative or were not encouraged sufficiently in their early postoperative exercises.

The use of heparin sodium and dicumarol<sup>®</sup> has been urged as a prophylactic measure but would seem to us too dangerous for general use (Ochsner and DeBakey,<sup>1</sup> Barker and others<sup>6</sup> and DeTakats and Fowler<sup>7</sup>). The use of these drugs in treatment has been extensive, but there are dangers, especially that of severe or fatal hemorrhage, as in Moses' 2 cases,<sup>8</sup> and the action of the drugs is difficult to control. Fur-

4. Dock, W.: The Use and Abuse of Bed Rest: Conferences on Therapy, New York Hospital, N. Y. State J. M. **44**:724, 1944.

5. Frykholm, R.: Pathogenesis and Mechanical Prophylaxis of Venous Thrombosis, Surg., Gynec. & Obst. **71**:307, 1940.

6. Barker, N. W.; Hygaard, K. K.; Walters, W., and Priestley, J. T.: A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism: Predisposing Factors, Proc. Staff Meet., Mayo Clin. **16**:1, 1941.

7. DeTakats, G., and Fowler, E. F.: The Problem of Thrombo-Embolism, Surgery **17**:153, 1945.

8. Moses, W. R.: Ligation of Inferior Vena Cava or Iliac Vein, New England J. Med. **235**:1, 1946.



thermore, they do not definitely prevent pulmonary emboli, even with adequate dosage, as stated by Ochsner and DeBakey<sup>1</sup> and as shown in our case 1. In the group of men who oppose their use are Moses,<sup>8</sup> Homans,<sup>9</sup> and Fine and Starr.<sup>10</sup> Those who favor their use include Barker, Nygaard, Walters and Priestley,<sup>6</sup> and de Takats and Fowler.<sup>7</sup> Our own feeling is that they are a valuable adjunct, to be used only with great care and with an excellent laboratory service available.

### HISTORY

Apparently the first ligation of the inferior vena cava was performed accidentally by Kocher in 1883 and was recognized only at postmortem examination. The first intended ligations were necessitated by operative injury to the vena cava; Trendelenburg's 3 cases (Trendelenburg,<sup>11</sup> Moses<sup>8</sup> and Miller<sup>12</sup>) of ligation for pelvic thrombophlebitis were exceptions. Only 1 of these 3 patients survived. Eighteen cases were collected by Pleasants<sup>13</sup> in 1918. Excellent reviews were made by Petit<sup>14</sup> in 1926 (11 cases with 4 deaths), by Wakefield and Mayo<sup>15</sup> and by Krotoski<sup>16</sup> in 1937. Our own review of the literature as available is briefly outlined in table 2.

### INDICATIONS AND RESULTS

As in most surgical conditions, there are a few absolute indications and contraindications for a certain procedure, with a middle ground where strong difference of opinion exists.

The absolute indications for ligation of the inferior vena cava, in addition to injury to the vein, appear to be the following: (1) pelvic thrombophlebitis or infected thrombi (Collins, Jones and Nelson,<sup>17</sup>

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9. Homans, J.: Deep Quiet Venous Thrombosis in the Lower Limb: Preferred Levels for Interruption of Veins; Iliac Section or Ligation, Surg., Gynec. & Obst. **79**:70, 1944.

10. Fine, J., and Starr, A.: Surgical Therapy of Thrombosis of the Deep Veins of the Lower Extremities, Surgery **17**:232, 1945.

11. Trendelenburg, F.: Ueber die chirurgische Behandlung der puerperalen Pyämie, München. med. Wchnschr. **49**:513, 1902.

12. Miller, C. J.: Ligation or Excision of Pelvic Veins in Treatment of Puerperal Pyemia, Surg., Gynec. & Obst. **25**:1431, 1917.

13. Pleasants, J. H.: Obstruction of the Inferior Vena Cava: Report of Eight Cases, Johns Hopkins Hosp. Reports **16**:363, 1911.

14. Petit, J.: Des plaies opératoires de la veine cava inférieure, J. chir. rev. critique **9**:153 (July-Dec.) 1912.

15. Wakefield, E. G., and Mayo, C. W.: Obstruction of Vena Cava Distal to Renal Veins, J. Missouri M. A. **31**:92, 1934.

16. Krotoski, J.: Zur Venenunterbindung bzw. -extirpation bei der puerperalen Allgemeininfektion vom chirurgischen Standpunkt, Chirurg. **9**:425, 1937.

17. Collins, C. G., Jones, J. R., and Nelson, E. W.: Surgical Treatment of Pelvic Thrombophlebitis: Ligation of Inferior Vena Cava and Ovarian Veins; Preliminary Report, New Orleans M. & S. J. **95**:324, 1943.

Ochsner and DeBakey,<sup>1</sup> Ochsner,<sup>18</sup> Kern and Berman,<sup>19</sup> and Moses<sup>8</sup>); (2) saddle thrombi, and (3) emboli following bilateral ligation of the femoral artery (Gaston and Folsom<sup>20</sup>). Moses stated that the inferior vena cava should be ligated for thrombophlebitis of the pelvis with "pulmonary embolus associated with prostatic tenderness of recent, or presumably recent, origin, especially with demonstration of deep tenderness along the anterolateral region of the rectum; reasonably conclusive evidence of pulmonary infarcts the source of which remains obscure despite diligent search; and venous occlusion of the lower extremities that would otherwise be treated by interruption of the femoral vein alone. The conditions governing the last are as follows: cellulitis or lymphangitis of the upper thigh, infections of the groin or the finding of enlarged and tender inguinal or femoral-triangle lymph nodes; recurrent emboli following bilateral ligation of the femoral veins; femoral phlebothrombosis with tense edema extending above the knee; the operative findings of adherent clot on exposure of the femoral vein; and acute thrombophlebitis extending into the upper thigh clinically, with the presence of pulmonary embolism."

In contradistinction, there would seem to be little indication for this procedure in unilateral phlebothrombosis or in thrombophlebitis which has not extended beyond the femoral vein.

In our 2 cases, we observed certain signs which had not been stressed previously. With progression of the disease process, inguinal pain and then lower abdominal pain (both of which have been mentioned repeatedly in the literature) developed; the pain then rapidly extended high into the lumbar region and the loin. It was associated with pronounced tenderness in the same area, with muscular spasm and with hyperesthesia in the distribution of the lumbar dermatomes. Although we have no anatomic proof, it is our belief that these symptoms and signs indicate a spread of the occlusive process into the vena cava or the lumbar collateral veins and so are a direct indication for ligation of the vena cava.

It is particularly in those cases of silent emboli, bilateral involvement of the lower extremity and involvement of one or both iliac veins or associated inflammation of the thigh or groin (Moses<sup>8</sup>) that a difference of opinion exists. Recently, chronic, deep phlebitis with edema of the legs has become an additional indication for ligation of the vena cava (Burton and Collier<sup>21</sup> and Kern and Berman<sup>19</sup>).

18. Ochsner, A.: *Intravenous Clotting, Surgery* 17:240, 1945.

19. Kern, H. M., and Berman, E.: *Ligation of Inferior Vena Cava for Pneumonic Thrombophlebitis*, *Am. J. Surg.* 69:120, 1945.

20. Gaston, E. A., and Folsom, H.: *Ligation of Inferior Vena Cava for Prevention of Pulmonary Embolism: Report of Two Cases*, *New England J. Med.* 233:229, 1945.

21. Burton, R. W., and Collier, F. A.: *Surgical Treatment of Long Standing Deep Phlebitis of the Leg*, *Surgery* 18:663, 1945.

Moses,<sup>8</sup> O'Neil<sup>22</sup> and Northway and Burton<sup>23</sup> stated the belief that ligation of the vena cava is indicated in cases of silent emboli, whereas Homans<sup>9</sup> was opposed, preferring bilateral ligation of the femoral vein. It must be remembered that bilateral thrombus formation occurred in a high percentage of cases; Neuman<sup>24</sup> recorded 52 per cent in postmortem studies. In the series of 202 cases recorded by Allen and others,<sup>25</sup> 78 per cent of ligations of the femoral vein were bilateral, and Fine and Starr<sup>10</sup> advocated routine bilateral ligation of the femoral vein. Concerning extension of the bilateral involvement to the inguinal ligament or above, opinion favored ligation of the vena cava (Homans,<sup>9</sup> Wakefield and Mayo<sup>15</sup> and O'Neil<sup>22</sup>).

It is our belief that even with involvement of one iliac vein ligation of the vena cava is the procedure of choice; this was the opinion of Moses,<sup>8</sup> Wakefield and Mayo<sup>15</sup> and O'Neil.<sup>22</sup> It was opposed by Homans,<sup>9</sup> Fine and Starr<sup>10</sup> and Veal and Hussey,<sup>26</sup> who stated that ligation of the iliac vein was indicated. The primary reason for ligation of the iliac vein is fear of a reduction in venous return after ligation of the vena cava; this has been fairly well disproved. O'Neil<sup>22</sup> stated that the collateral circulation after ligation of the vena cava is in effect as adequate as that after ligation of the common iliac vein: "The collateral pathways available after ligation of the lower vena cava fall roughly into three groups—the superficial, the deep, and those of the ascending lumbar trunks. The first of these comprise the superficial circumflex iliac and the superficial epigastric veins, which connect the saphenous system with the superficial thoracic veins and those of the upper abdominal wall. The deep pathways are formed by the anastomosis of the deep circumflex iliac, superior epigastric and lumbar veins, thereby connecting the external iliac veins with the internal mammary and ascending lumbar veins. The ascending lumbar trunks begin in the pelvis on either side of the promontory of the sacrum and communicate with the sacral common iliac, hypogastric and iliolumbar veins. . . . The right lumbar trunk becomes the azygos vein and terminates in the superior vena cava; the left continues as the hemiazygos vein and eventually enters the right azygos vein." Experiments with injection

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22. O'Neil, E. E.: Ligation of the Inferior Vena Cava in Prevention and Treatment of Pulmonary Embolism, *New England J. Med.* **232**:641, 1945.

23. Northway, R. O., and Burton, R. W.: Ligation of Inferior Vena Cava, *Surgery* **18**:85, 1945.

24. Neumann, R.: Ursprungszentren und Entwicklungsforsmen der Bein thrombose, *Virchows Arch. f. path. Anat.* **301**:708, 1938.

25. Allen, A. W.; Linton, R. R., and Donaldson, G. A.: Thrombosis and Embolism: Review of Two Hundred and Two Patients Treated by Femoral Vein Interruption, *Ann. Surg.* **118**:728, 1943.

26. Veal, J. R., and Hussey, H. H.: Deep Venous Thrombosis of the Lower Extremities, *Surgery* **17**:218, 1945.

by Bohner, Poirer and Goleman, cited by Kern and Berman,<sup>19</sup> showed that after ligation of the vena cava the blood is returned to the heart without difficulty; this fact was confirmed in our case 1 by a roentgenoscopic examination after the administration of iodopyracet injection. Northway and Burton,<sup>23</sup> using injection methods in the study of cadavers, observed the more important collateral pathways and proved that they were obviously adequate. (The principal anastomotic channels are veins in and about the spinal canal, the groin and the azygos veins.)

In Northway and Burton's 10 cases in which ligation was done, any edema of the legs which persisted was well controlled with elastic bandages; the degree of immediate postoperative edema was minimal. Moses<sup>8</sup> stated that whenever edema follows ligation of the vena cava or the iliac vein there is unequivocal evidence of either persistence or recurrence of the disease process. He also stated the belief that edema of the leg is less severe after ligation of the vena cava than after ligation of the femoral vein. Kern and Berman's patient<sup>19</sup> was free of edema on the sixteenth day; later, he was able to work as a policeman without discomfort, edema or the necessity for an elastic stocking. Others supported this evidence with case reports (O'Neil,<sup>22</sup> Gaston and Folsom,<sup>20</sup> Pfaff<sup>27</sup> and Veal and Hussey<sup>26</sup>). Further studies on venous pressure by Collins, Jones and Nelson<sup>17</sup> showed a rapid fall in venous pressure in the first weeks after ligation. In our 2 cases, edema disappeared in eleven and ten days, respectively. In support of Moses' contention,<sup>8</sup> the patient in case 1 showed rapid subsidence of the swelling in the first leg involved; there was slightly increased edema of the other leg, evidently due to its thrombotic involvement, but this also subsided (over a period of twelve days) until the leg was smaller than it had been before the operation (table 1).

Another factor in favor of ligation of the vena cava rather than of one iliac vein is the high incidence of bilateral involvement. Ligation of the vena cava prevents the formation of an embolism from the other leg. Veal and Hussey<sup>26</sup> reported 3 cases in which death occurred from this cause. Since the two procedures are similar in time, skill and amount of anesthesia necessary as well as in risk, ligation of the vena cava seems the procedure of choice. Actually, to us, it seems an easier procedure, especially if the left iliac vein is involved. Hershey and Bailey<sup>28</sup> used ligation of the vena cava in their case because of the patient's poor condition, and stated that they ordinarily would have used ligation of the iliac vein. If it is used in cases of poor risk

27. Pfaff, O. G.: Ligation of Inferior Vena Cava, *Am. J. Obst. & Gynec.* **11**:660, 1926.

28. Hershey, C. D., and Bailey, R. D.: Management of Thrombophlebitis, *West Virginia M. J.* **42**:1, 1946.

because it is easier, why should it not be used in all cases? Veal and Hussey<sup>26</sup> reported 4 cases in which the formation of recurrent pulmonary emboli followed ligation of the femoral vein through a diseased segment, and other cases in which a thrombus formed above the point of ligation and extended into the inferior vena cava, making a secondary and more hazardous operation necessary. Certainly, primary ligation of the vena cava would seem the most conservative operation in such cases. Apparently no deaths occurred in the 6 cases of ligation of the vena cava reported by Veal and Hussey; there were 7 among 76 other cases.

So far as the operative technic itself is concerned, we favor the transperitoneal approach for its simplicity. A short transverse or midline incision should be used in order to save the inferior epigastric vessels for collateral circulation. The intestines are packed away. A short incision is made through the posterior peritoneum overlying the vena cava, the peritoneum is stripped off and a curved instrument is passed around the vein with the ligature, which is then slowly drawn tight. In each case, the ligation was made just above the last lumbar vein. It is easier here, and we thought that the presence of the lumbar vein below the ligature might assist in the formation of late collateral circulation. Umbilical tape was used, but any suture large enough to prevent cutting of the vein will suffice. The advantages of this approach over the retroperitoneal approach are: (1) ease of observation of pathologic features, (2) preservation of all the lumbar veins for collateral circulation (they may be torn or traumatized in the retroperitoneal approach), (3) performance of the procedure entirely under direct vision and (4) ease of performance of a lumbar sympathectomy, if it is indicated.

Any anesthesia indicated for the patient is satisfactory. In our cases, a 1 per cent solution of procaine hydrochloride was used locally because of the patient's extremely poor condition.

#### SUMMARY

Thrombosis, either postoperative or occurring in the course of medical diseases, is a serious complication, primarily because of the frequent deaths due to pulmonary embolus and secondarily because of the residual edema and ulceration of the leg. The prevention of thrombosis is made possible in most instances by careful prophylactic measures, including the maintenance of fluid balance, the prevention of stasis, the prevention of shock and, in surgical cases, the use of technic to minimize damage to the tissues. The use of conservative measures, as indicated, will prevent any serious complication in most instances. These should include the immobilization and elevation of the leg and the use of a heat cradle, supporting (elastic) bandages and perhaps, sympathetic nerve blocks. We feel that the use of anticoagulant drugs

is indicated in a certain percentage of cases. Surgical measures will be necessary in a small percentage of cases, including ligation of the femoral vein of either type, as indicated, and rarely, ligation of the iliac vein on the right side or of the vena cava. When the thrombosis has spread into the left iliac vein, or into either iliac vein with a possibility of involvement of the opposite leg, we believe that ligation of the vena cava is the procedure of choice. We believe that ligation of the vena cava is indicated in cases in which there is involvement of both legs to above the inguinal region and in cases of pelvic thrombophlebitis because of the ease of access, the lack of trauma to the tissues and the ease of observation of pathologic conditions.

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## SIGNIFICANCE OF THE SEROSAL ARTERIOLES IN RESUSCITATION OF THE SMALL BOWEL

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ON MANY occasions the surgeon is confronted with the problem of whether or not an intestinal segment is viable. This is especially true in emergency situations, as when an operation is performed for incarcerated and/or strangulated hernias or for intestinal obstruction. At the operating table valuable time elapses as the surgeon waits patiently to ascertain the return of a bowel loop to normalcy. Since most patients with these conditions are not the best operative candidates, the additional period of anesthesia and exposure of the peritoneal cavity to the atmosphere increases the morbidity. Often this delay, lingering and waiting, is a major factor in producing death.

Thus a rapid diagnostic criterion of viability of the small bowel is of practical importance. Observation at the operating table in this type of situation has brought to light such a criterion. In addition to the clinical observation, experimental evidence in animals is offered in support of it.

The final test of whether or not a loop of small intestine is viable depends primarily on the blood supply to that loop. A basal blood supply which can maintain the nutritional state of the intestinal wall is sufficient to preserve viability. This blood supply may be adequate even in the presence of local intestinal cyanosis, congestion and inhibited peristalsis. Obstructed loops of small intestine have a remarkable inherent potentiality of returning to normal. However, in the presence of advanced thrombosis in the mesenteric vessels, or bowel asphyxia, resuscitation is impossible. Therefore a correct indicator of adequate blood supply to the bowel segment is the all-important determinator. This determinator enables the observer to know that resuscitation of the bowel will occur even in the presence of marked congestion, discoloration and inhibition of peristalsis. Hence, if this indicator is adequate, a questionable intestinal loop may be redeposited immediately into the peritoneal cavity without undue fear of perforation.

It is believed that a satisfactory determinator of this type is available to the surgeon at the operating table. This indicator is visible by direct investigation of the vascular tree. The point of observation is the most

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distal circumference of the small intestine on the antemesenteric border. The serosal arterioles are examined for their red color and the presence or absence of pulsations. These vessels in normal intestine are not as prominent as they are in the obstructed loop with secondary venous congestion. The venous congestion increases the arteriolar pressure so that the vessels become extremely prominent. If pulsations are visible in the small arterioles on the antemesenteric border and if the red color of the circulating blood can be seen, the bowel is viable. This is true

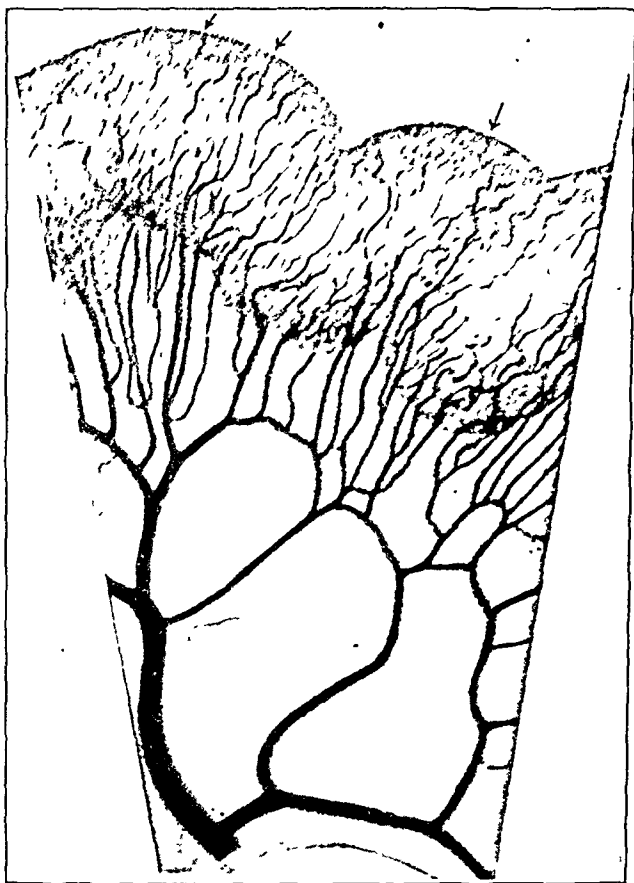


Fig. 1.—Injected arteries of human ileum demonstrating the rich vascularity of the small bowel. Arrows indicate the point of observation in the determination of the viability of the intestinal segment.

even if the intestinal wall is markedly darkened from edema and congestion and even if the blue-black color of the intestine is prominent.

The rationale of this observation resides in the fact that if there is adequate arterial circulation and venous return in the most distal area of the intestine the circulation must be satisfactory in the more proximal areas. Where there is adequate arterial circulation, there is also adequate oxygenation with a satisfactory nutrition supply to the tissue under



Fig. 2.—Intestinal loop demonstrating the return to normal of an obstructed segment of bowel in a rabbit. Serosal arterioles are visible, indicating adequate blood supply.



observation. Adequate oxygenation and nutrition of the segment are the basic necessities for intestinal viability. Both these physiologic functions depend on a sufficient arterial circulation. Therefore, when an adequate circulation is present, the intestine must, of necessity, be viable. This criterion has been followed on many occasions at the operating table without any serious complications occurring which could be attributed to the intestinal segment under observation.

In order to substantiate this clinical observation, experimental evidence is offered in its support. The animals employed for study were rabbits in whom occlusion of the blood supply to intestinal segments was artificially induced. Strangulation of the intestine was allowed to progress until the arterioles of the antemesenteric border became prominently visible. The intestine became blue-black and congested, and peristalsis was inhibited. When this point was reached, the blood supply was allowed to return, and the intestinal loop regained its former appearance. The rabbit's abdominal wall was sutured, and each animal had an uneventful recovery. This procedure was performed in 3 different rabbits.

The same procedure of obstructing an intestinal loop was performed with the exception that strangulation of the bowel was allowed to continue beyond the preservation of the arteriolar blood supply. Obstructed segmental loops of this type could not and did not return to normal. This is the type of strangulated intestine which goes on to perforation producing peritonitis. Three rabbits were treated in this fashion. All died. Autopsy revealed generalized peritonitis secondary to intestinal gangrene with perforations. Thrombotic processes were evident in the vascular tree of the segments involved.

This experimental evidence and clinical observation on strangulation of the small intestine has unfolded a diagnostic criterion of determining the viability of strangulated intestine in the operating room. This criterion enables the surgeon to save valuable time as he attempts to determine the viability of obstructed intestinal loops. Furthermore, it will decrease the period of exposure to which the peritoneal cavity may be subjected. This factor may be the deciding point in the preservation of life in a patient who is already debilitated by a physiologic imbalance secondary to an intestinal obstruction.

#### SUMMARY AND CONCLUSIONS

1. The need for a decisive, rapid method of determining the viability of small intestine is emphasized.
2. Clinical observation and animal experimentation have supplied a criterion to answer this need.
3. The criterion in question concerns the serosal arterioles on the antemesenteric border of the small bowel.

4. Adequate circulation in these vessels indicates viability of the bowel even in the presence of discoloration, edema and inhibition of peristalsis.

5. Employing this criterion, the surgeon has available a rapid indicator which will save valuable time in determining the integrity of intestinal loops.

This procedure has been followed without any resulting complication which can be attributed to the unreliability of the diagnostic criterion. It is therefore advocated as a safe and sound method of determining intestinal resuscitation.

# PROGRESS IN ORTHOPEDIC SURGERY FOR 1946

A Review Prepared by an Editorial Board of the American Academy  
of Orthopaedic Surgeons

## XIX. FRACTURES

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IN 1946, the first postwar year, the number of articles on fractures increased and the emphasis shifted from gunshot fractures to more nearly normal interests. Intramedullary fixation continued to attract more attention and represented the principal change in the management of fractures. The use of antibiotic drugs became so general that little more was said about their use in compound wounds. External devices for skeletal fixation were mentioned much less frequently as vitallium plates and screws and "18-8 S M O" stainless appliances came to be recognized for their dependability. But still unsettled were the many questions raised concerning conservative vs. operative treatment of fractures.

### FRACTURES OF THE SHOULDER

McBride<sup>868</sup> makes the point that shoulder injuries are not always easy to diagnose and may be confused with lesions of the cervical portion of the spine. Consequently, the diagnosis must be well established before any plan of treatment is undertaken.

Dor<sup>869</sup> had the experience of reducing dislocations of the shoulder in several hundred cases by a simple maneuver, without anesthesia. While he explained to the patient that he was only making an examination, the elbow was brought forward while the wrist was pushed outward; often there was a click as the shoulder fell in place. Sometimes

868. McBride, E. O.: *Shoulder Wounds and Injuries*, New Orleans M. & S. J. 98:533-541 (June) 1946.

869. Dor, J.: *Reduction of Recent Anterior-Internal Luxations by Slow Rotation*, *Rev. d'orthop.* 32:197-198 (May-Aug.) 1946.

several repetitions of the maneuver were required before the shoulder was reduced. As the author explains, the method is recommended only for use in cases of recent fracture and after preliminary roentgenographic examination.

A case of bilateral dislocation of the shoulder is reported by Lynn and Peterson.<sup>870</sup> The patient, a navigator on a bomber, was propelled between the seats of the pilot and the co-pilot in a crash landing, sustaining bilateral subcoracoid dislocation. The patient was treated two months' after injury by open reductions and Nicola fixation. Preliminary traction for eighteen days on the left shoulder made the operation easier than on the right side, on which no preliminary traction was used. Active motion was started one month after the second operation (seven weeks after the first). Abduction and flexion to 90 degrees bilaterally, with moderate restriction of rotation, was obtained.

Smith<sup>871</sup> reports a rare type of posterior dislocation of the shoulder in a frail woman, of 88, who fell forward without having the arm extended. Arthritic changes present in the joint may have facilitated the displacement, which was easily recognized by palpation and was corrected by the usual Kocher maneuver. In those cases in which the condition is not recognized, a good, functional false joint is established behind the glenoid cavity.

Hart<sup>872</sup> recommends that irreparably injured shoulders be immobilized in a plaster spica, the following factors obtaining: (1) 60 to 70 degrees of abduction; (2) 45 degrees of forward flexion; (3) normal position of the scapula; (4) sufficient external rotation at the shoulder so that the hand is on a level with the chin; (5) extension of the shoulder spica from the crease of the palm to just above the trochanters, so that the spica rests firmly on the pelvis; (6) inclusion in the spica of a strap of plaster over the normal shoulder, and (7) prevention of pressure on the ulnar nerve or the median epicondyle.

*Fractures of the Scapula.*—Pelloja<sup>873</sup> states that isolated fractures of the acromion are rare. In cases involving young persons, the confusing point in diagnosis is the fact that the epiphysis does not fuse until 20 to 25 years of age. In reports of 2 cases, the author describes the treatment of lateral fractures by lifting and abducting the shoulder.

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870. Lynn, T. A., and Peterson, L. T.: Bilateral Simultaneous Dislocations of Shoulders, *J. Bone & Joint Surg.* **28**:161-163 (Jan.) 1946.

871. Smith, A. M.: Subacromial Dislocation of the Shoulder, *Brit. M. J.* **2**:694-695 (Nov. 9) 1946.

872. Hart, V. L.: Immobilization of Irreparably Injured Shoulder Joint, *Bull. U. S. Army M. Dept.* **5**:366 (March) 1946.

873. Pelloja, M.: Isolated Fractures of the Acromion, *Arch. ital. chir.* **67**:140-146, 1945.

A case of bilateral fracture of the scapula is reported by Heatly, Breck and Higginbotham.<sup>874</sup> One scapula was treated by strapping with adhesive tape, but the other required insertion of skeletal traction along the vertebral border and counter traction through adhesive tape on the arm. Satisfactory, though not perfect, reduction was obtained; the functional result was excellent.

*Acromioclavicular Dislocation.*—Simple strapping of the acromioclavicular joint was used by Goldberg<sup>875</sup> in 53 cases; all patients were able to return to duty within four weeks. Adhesive tape was passed over a pad on the outer end of the clavicle and down around the padded olecranon; the arm was then fixed to the chest with tape. The patients were thus immobilized from four to fourteen days or until all tenderness had subsided.

Gibbens<sup>876</sup> describes a special type of cast to hold the acromioclavicular joint after dislocation and reduction. A cast is placed on the arm, and two aluminum extension bars are attached to the top of the cast. An elastic strap over the end of the clavicle is fastened to the extension bars in the cast. Results were satisfactory in 10 cases.

Stewart<sup>877</sup> reports 9 cases of acromioclavicular separation; treatment was with the Bosworth vitallium screw, inserted through the clavicle and into the coracoid process.

[Ed. NOTE (W. G. S.).—As these articles indicate, there is still no generally accepted treatment for acromioclavicular separation. Strapping, the use of casts, screws, wire or fascial loops and resection of the end of the clavicle are still in vogue with various surgeons. Fortunately, the ill effects of this injury are not particularly disabling.]

*Fractures of the Clavicle.*—Van Demark and Goodman<sup>878</sup> stress that in treating fracture of the clavicle in soldiers, it is extremely important to secure exact reposition of the fragments. Otherwise the irregular fracture site will be irritated by shoulder straps, rifles and other military equipment. Therefore the authors followed a policy of treating the patients in bed, with lateral traction on the arm for five weeks. Even so, it was sometimes necessary to manipulate the fragments under anesthesia.

874. Heatly, M. D.; Breck, L. W., and Higginbotham, N. L.: Bilateral Fracture of the Scapulae, *Am. J. Surg.* **71**:256-259 (Feb.) 1946.

875. Goldberg, D.: Modified Conservative Treatment of Acromio-Clavicular Joint Injuries, *Am. J. Surg.* **71**:529-531 (April) 1946.

876. Gibbens, M. E.: Appliance for Conservative Treatment of Acromio-Clavicular Dislocations, *J. Bone & Joint Surg.* **28**:164-165 (Jan.) 1946.

877. Stewart, R.: Internal Fixation of Clavicle and Coracoid Process with Vitallium Screw, *Minnesota Med.* **29**:357 (April) 1946.

878. Van Demark, R. E., and Goodman, M. C.: Clavicle Fractures in Military Trainees, *Mil. Surgeon* **99**:197-199 (Sept.) 1946.



Mbuthia and Kisali<sup>879</sup> treated 300 patients with fracture of the clavicle with figure 8 plaster bandage, applied while the shoulders were held in extension. Temporary symptoms of pressure on the nerve developed in only 1 case.

Goumain and Labarbe<sup>880</sup> describe a method of internal fixation of the clavicle by insertion of a Kirschner pin through a transcutaneous approach. For fixation of a fracture near the outer extremity of the clavicle a puncture wound is made in the skin, and, through it, an oblique opening is made in the clavicle, about 6 cm. from the sternoclavicular joint. The hole is directed backward and outward. After reduction a Kirschner pin, 10 cm. in length, is inserted under radioscopic control, to the peak of the first curvature. If the end of the pin extends beyond the entry hole, it is withdrawn slightly, cut off properly and driven in flush with the bone. The shoulder is mobilized on the second or third day, using a sling. For treatment of fractures of the inner end of the clavicle, the pin is inserted from the acromial end.

Bermudez and Odam<sup>881</sup> state that they treat fractures of the clavicle by reduction under local anesthesia, with the patient in a sitting position. Traction is applied with a knee, between the shoulders, and the clavicle is immobilized by the use of prepared loops of bandage, passed over axillary pads and acromial pads without compression. The arm on the injured side is kept in a sling for about twenty-five days. "The result, though not always perfect reduction, is excellent function."

Lee<sup>882</sup> used a nail, driven in from the outer end of the clavicle through an incision along its upper border, to secure reduction in a case in which repeated attempts at closed reduction had failed. No retention was used. The nail was removed in six weeks, and the result was perfect.

Cobey<sup>883</sup> describes a method used for eleven years with no unfavorable complications. In about 14 per cent of cases in which reduction could not be maintained, an incision was made over the fracture and the fragments were held together with towel clips, forced into the bone. The handles of the towel clips were fastened to each other with a wooden block.

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879. Mbuthia, A. S., and Kisali, J.: Treatment of Fracture of the Clavicle by Plaster of Paris Bandages, *East African M. J.* **23**:154-155 (May) 1946.

880. Goumain, A. J. M., and Labarbe: Transcutaneous Intramedullary Fixation of Fractures of the Clavicle with Kirschner Pin, *Bordeaux chir.* **3-4**:75-80 (July-Oct.) 1943.

881. Bermudez, E., and Odam, J.: Conservative Procedure in Therapy of Fractures of the Clavicle, *Gac. méd., Lima* **1**:168-169 (June) 1945.

882. Lee, H. G.: Treatment of Fracture of Clavicle by Internal Fixation with Nail, *New England J. Med.* **234**:222-224 (Feb. 14) 1946.

883. Cobey, M. C.: Towel Clip Fixation of Fresh Clavicular Fractures, *South. M. J.* **39**:307-311 (April) 1946.

[ED. NOTE (W. G. S.).—Of course, most fractures of the clavicle are uncomplicated, and the usual conservative treatment is adequate. Moreover, nonunion is extremely rare in the clavicle, and union in practically any position will give a well functioning shoulder. Therefore, operative treatment should be reserved for the unusual or irreducible fracture of the clavicle.]

#### FRACTURES OF THE UPPER EXTREMITY

In a comprehensive article, Fitts<sup>883a</sup> presents a digest of treatment of fractures of the upper extremity, gathered chiefly from seventy-seven articles listed in the bibliography. The salient points are: 1. Fractures of the upper extremity in World War II were treated by ambulatory methods. 2. War experience has emphasized that the functioning of the joints of the upper extremity should be subservient to the proper functioning of the hand. 3. Fractures of the humerus were best handled with the arm near the body, and the efficiency of the "hanging cast" was established. 4. A high incidence of fractures of the carpal scaphoid was encountered, good results being obtained by prolonged immobilization if instituted early. 5. Fingers immobilized in extension showed a high incidence of stiffness, indicating that positions of flexion should be used and that the uninjured fingers must not be immobilized. 6. Injuries to nerves and blood vessels were frequent in compound fracture of the upper extremity, and treatment of these injuries often took precedence over treatment of the fracture.

*Fractures of the Humerus.*—Jones<sup>884</sup> has used a metal abduction splint for fractures of the upper two thirds of the humerus for more than twenty years. It is very light, being made of duralumin, and can be bent easily to conform to the arm and body. Only a slight amount of abduction is needed to correct most deformities of the humerus, and this splint is sufficient in more than 90 per cent of cases.

Kandel<sup>885</sup> discusses the anatomy and function of the normal shoulder and includes a lengthy section on the roentgenography of the region; the types of fractures and of undetermined fractures or dislocations are described from the point of view of a radiologist. The mechanism of the fracture, such as direct blow, torsion or compression, is then discussed. The author states the belief that the mechanism of displace-

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883a. Fitts, W. T., Jr.: Fracture of Upper Extremity: Review of Experiences in World War II, *Am. J. Surg.* **72**:393-403 (Sept.) 1946.

884. Jones, L.: Simple Conservative Method of Treatment of Fractures of the Upper End of the Shaft of the Humerus, *Surg., Gynec. & Obst.* **83**:126-128 (July) 1946.

885. Kandel, B.: Fractures and Fracture Luxations of the Upper End of the Humerus, *Semana méd.* **1**:422-447 (March 7) 1946.

ment is due to muscular action; there is a long, detailed section on the manner in which this factor acts.

A discussion of the use of Caldwell's "hanging cast" for treatment of fractures of the humerus is presented by Paredes.<sup>886</sup> The article is devoted to an exposition of the advantages of the method, a review of the muscles inserted on the humerus and the effect of these muscles on fractures at different levels. The author lists the types of fractures to which the method is adapted and those in which it should not be used. The manner of applying the cast is described. The contraindications for this method are: (1) combined fracture and dislocation of the humeral head; (2) complete avulsion of the tuberosity; (3) fracture of the neck, with rotation of the head; (4) open fractures, and (5) fractures with interposition of the soft parts between the bone fragments.

Laurence<sup>887</sup> stresses his dislike for traction and casts in treatment of fractures of the humerus and recommends the use of intramedullary Kirschner wires. The results of this treatment in 6 cases were excellent.

Debeyre and Rene<sup>888</sup> treated 2 patients with fracture of the surgical neck of the humerus by inserting a long Smith-Petersen nail through the top of the head of the humerus. In each case, the nail was removed two months after insertion and good functional results were noted.

Bloom<sup>889</sup> has similarly utilized multiple Kirschner wires to immobilize fractures near the head of the humerus. With the arm in mid-position, the head of the humerus is anchored by forcing a removable Steinmann pin through the acromion and into the head. Then, with roentgenoscopic observation, the distal fragment is manipulated until the fracture is reduced. Kirschner wires are drilled through the anterolateral surface of the distal fragment, up the medullary space and into the head. Two wires are usually sufficient to hold the fragments. The method was used in 4 cases.

*Supracondylar Fractures of the Humerus.*—Finck<sup>890</sup> reports 9 cases of malunited supracondylar fracture, in which he explored the frac-

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886. Paredes, J. J.: Therapy by Means of Hanging Cast: Fracture of Humerus, *Amatus* **5**:162-172 (Feb.-March) 1946.

887. Laurence, G.: Intramedullary Kirschner Nail in Treatment of Fractures of the Humerus, *Rev. d'orthop.* **32**:81-87 (Jan.-April) 1946.

888. Debeyre, M., and Rene, J.: Osteosynthesis with Smith-Petersen Pin in Fractures of the Surgical Neck of the Humerus, *Rev. d'orthop.* **32**:194-196 (May-Aug.) 1946.

889. Bloom, F. A.: Treatment of Fractures About the Surgical Neck of the Humerus with Closed Reduction and Blind Pinning, *M. Rec.* **40**:1494-1495 (July) 1946.

890. Finck, C.: Supracondylar Fractures in Children, *Torreón méd.* **1**:101-120 (May-June) 1946.

ture, excised the callus and new bone, replaced the fragments in normal position and sutured the soft tissues, without any sort of internal fixation.

Sorrel and Longuet<sup>891</sup> describe an anterior incision for exposure of the rare anterior displacement of supracondylar fractures. The authors have used the method in 11 cases and find it valuable in determining the amount of damage to muscles, nerves and blood vessels.

A method of applying traction in bed for patients with supracondylar fractures, known as the Zeno method, is discussed by Riosalido.<sup>892</sup> It consists of the insertion of a Kirschner wire through the olecranon, with application of traction horizontally on the olecranon and vertically on the hand. After a few days to permit reduction of overriding, a band is applied around the upper arm, above the fracture site, and a cast is eventually applied over the traction apparatus when roentgenography shows proper reduction.

[ED. NOTE (P. L. N.).—This method of traction is not without danger, as the ulnar nerve may be transfixed during application. Landmarks about the elbow are not easily palpated when the joint is disorganized and badly swollen.]

A series of 47 cases of supracondylar fractures of the humerus in children is reported by LeCocq and Slade.<sup>893</sup> Twenty-five patients were treated by the Dunlop method of traction, with the elbow at an angle of 30 to 40 degrees and with countertraction downward applied just proximal to the elbow. The authors state that gentle manipulation guides the fragments into position when all traction is in place. As a rule complete reduction is shown by roentgenographic check-up in forty-eight to seventy-two hours. One of the main advantages is the avoidance of Volkmann's ischemia, which may result from the classic reduction with the elbow in acute flexion. Traction is maintained for two to three weeks and is then replaced by a plaster mold, with the elbow in flexion at a little more than a right angle. After five weeks a sling is used, and motion is gradually instituted. Of the 25 patients treated by this method, 16 experienced excellent results, with no limitation of movement or residual deformity. Four patients had within 10 degrees of normal motion, and 5 experienced fair results (not within 10 degrees of normal motion).

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891. Sorrel, E., and Longuet, Y. J.: Anterior Transbrachial Route in Surgery of Supracondylar Fractures in Children, *Rev. d'orthop.* 32:117-142 (May-Aug.) 1946.

892. Riosalido, M.: Zeno Traction in Therapy of Supracondylar Fractures, *Actas Soc. de cir. de Madrid* 5:187-197 (April-June) 1946.

893. LeCocq, J. F., and Slade, I.: Treatment of Supracondylar Fractures in Childhood, *Northwest Med.* 45:30-32 (Jan.) 1946.

[ED. NOTE (P. L. N.).—This is a proved and highly satisfactory method of treatment. It is preferable to repeated manipulations.]

A detailed discussion of various types of supracondylar fractures of the humerus, including dicondylar fractures and the T and Y fractures at the distal end of the humerus, is given by Herzog.<sup>894</sup> There is extensive discussion of the clinical and roentgenologic findings, including injuries to the epiphyses and the associated soft parts. The author devotes considerable attention to the prognosis, which so often depends on the timeliness and correctness of the treatment. He discusses the types of fractures in 3 classifications: (1) the cases of slight injury, in which a simple plaster splint is made after correct manual reduction; (2) the cases of severe injury, and (3) the cases of extremely severe damage. In the latter two types, he recommends wire extension on the ulna as the ideal procedure. In addition, there is discussion of other methods of treatments of fractures and of the treatment of residual injuries, such as paralysis of nerves and deformities of the bones, resulting partly from the nature of the fracture and also from improper treatment.

An extensive study of 163 cases of fracture of the lower end of the humerus, in which the patients were treated at the Crown Princess Louise Hospital in Stockholm, is reported by Holmberg.<sup>895</sup> The fractures were classified as "horizontal" (supracondylar or dicondylar) in 142 cases; in 17 cases, the fracture was through the lateral condyle, and in 4, it was through the medial condyle. In 87 of the horizontal fractures, the distal fragment was dislocated backward. Forward dislocation occurred in only 3 cases. A combined dislocation, backward and toward the radius and ulna, often occurred. Rotation between the fragments occurred in 2 cases. The left arm was injured in 61 per cent of the cases. Holmberg concludes that the reason for the poor results in cases in which either a higher degree of varus dislocation or limited mobility remained was the unsatisfactory coaptation of the fragments. Open reduction and fixation with nails is advocated when closed reduction cannot be accomplished.

*Injuries to the Elbow.*—A roentgenologic analysis of 328 fractures of the elbow, treated at the Centrallasarettet in Borås, Sweden, from 1932 to 1941, is presented by B. A. Nohrman.<sup>896</sup> The follow-up was 80 per cent complete, and the time of observation was two years or more after injury. Sixty-one per cent of the injuries involved the

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894. Herzog, H.: Supracondylar Fractures of the Humerus, *Helvet. med. acta* **11**:615-689 (Nov.) 1944.

895. Holmberg, L.: Fractures of the Distal End of the Humerus in Children, *Acta chir. Scandinav. (supp. 103)* **92**:1-69, 1945.

896. Nohrman, B. A.: Fracture in the Elbow with Particular Regard to Distal Humerus End, *Acta radiol.* **27**:409-415, 1946.

distal end of the humerus; 25 per cent, the head and neck of the radius; about 10 per cent, the ulna alone, and 6 per cent, both bones. In 13 per cent of cases, the fracture was combined with luxation. The average age of male patients was 15 years and that of female patients, 25 years. Forty-one per cent of the fractures occurred in adults; these consisted mostly of fractures of the radius and the ulna. The supracondylar fractures were the common injuries in children.

Seventeen cases of injuries resulting from throwing the javelin are reported by Waris.<sup>897</sup> During the first year of competition, the elbow of the throwing arm had in every instance become so painful that the subject was compelled to give up the sport for several weeks to a year. Injury recurred after two to three years. The elbow finally became so insensitive, after repeated injuries, that the subject was able to stand all the strain without pain. The clinical change in the elbow was very slight. Fourteen of 17 subjects showed roentgenologic changes. The majority of these changes were in the tip of the olecranon (in 11 cases). These consisted of different types of fractures in the olecranon and of ruptures of its tips.

Complete fracture of the olecranon, which had healed in a dislocated position, was noted in 3 cases. Rupture of the triangular tip of the olecranon was present in 2 cases, a free calcium shadow at the tip of the olecranon, in 4 and a rough, irregular outline of the tip, in 5.

When the elbow is suddenly straightened during the last stage of throwing the javelin, the tip of the olecranon strikes its fossa and stops the movement of extension. This violent blow is no doubt the cause of the changes in the olecranon. Calcification near the median epicondyle undoubtedly represents the subsequent formation of scars from the ruptures of the medial collateral ligaments and capsules.

The changes in the elbow were all extracapsular after-effects of a definite trauma; no changes resembling those mentioned in Baetzner's theory of arthritis deformans could be found.

[ED. NOTE (W. G. S.).—This is an interesting type of athletic injury, which occurs also in the elbows of baseball pitchers, as described by Dr. George Bennett, in 1945.]

Woods<sup>898</sup> describes a case of the extremely rare forward dislocation of the elbow in a sailor of 32 "in a state of alcoholic felicity." Roentgenograms revealed that there was no fracture and that the bones of the forearm were entirely anterior to the lower end of the humerus. Very strong traction was needed to overcome the dislocation, and after

897. Waris, W.: Elbow Injuries of Javelin Throwers, *Acta chir. Scandinav.* 93:563-575, 1946.

898. Woods, R. S.: Complete Forward Dislocation of the Elbow, *Clin. J.* 75:216-218 (Nov.-Dec.) 1946.

reduction was completed there was pronounced extravasation of blood in the soft tissues. Consequently, light massage and early motion were advised.

The treatment of "sideswipe fractures" (multiple fractures involving the left elbow, the result of the arm's projecting beyond the door of a car when it is sideswiped) is described by Highsmith and Phalen.<sup>899</sup> These fractures are difficult to treat because of the severe trauma to soft tissues; poor results are likely. Amputation may be necessary through the site of the humeral fracture when circulatory damage is pronounced. Débridement, approximation of fragments, immobilization and, later, if necessary, grafting of bone was the order of procedure in 7 cases.

An extensive article on resection of bone fragments in comminuted infected fractures of the elbow is presented by Nicholson.<sup>900</sup> A group of patients treated early in the campaign in the Solomon Islands by resection of fragments three to ten days after injury did very well. No follow-up was possible because of evacuation of the group. Later, 12 other patients with compound fractures involving the elbow joint, caused by bullet or shrapnel wounds, were operated on from two to six months after injury, and fragments were removed. Draining wounds existed at the time of operation in 11 of these cases. The cases were followed from one to seventeen months. There were no major complications after resection of fragments. The patients were allowed up with a sling on the second day after operation, and elbow motion was begun two weeks after operation. Primary closure of infected wounds was done when penicillin was available. Healing time of the wounds depended on the extent of soft tissue damage. Functional results were best when there was little loss of bone substance. In cases with preservation of the trochlear surfaces of the humerus and ulna, the elbow joint, to all intents and purposes, functioned normally. With loss of the olecranon or the condyle of the humerus the power of extension was sacrificed. The loss of trochlear surface in the ulna produced lateral instability in relaxation and a slight loss of power of flexion. Lateral instability of more than 45 degrees resulted in loss of the ability to abduct the extended arm. Resection of 2 or 3 inches (5 or 7.5 cm.) of the humerus resulted in a longer period before power of flexion was regained and in the least stable joints. The widest resection possible was considered to be 3 inches. The ability actively to supinate and pronate the forearm was

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899. Highsmith, L. S., and Phalen, G. S.: Sideswipe Fractures, *Arch. Surg.* **52**:513-522 (May) 1946.

900. Nicholson, J. T.: Compound, Comminuted Fractures Involving the Elbow Joint: Treatment by Resection of Fragments, *J. Bone & Joint Surg.* **28**:565-575 (July) 1946.

with 1 exception dependent on the absence of the radial head. Function was improved in 3 cases by secondary removal of the radial head. The only patient with supination deformity had not had the radial head removed. In all cases, pronation was more difficult to obtain than supination. A joint space did not redevelop at the site of the resected elbow, but fibrous scar tissue persisted between the bone ends six months after operation. Formation of bone spicules was observed but had not resulted in loss of function.

The results in 21 consecutive cases of fracture of the epiphysis of the medial epicondyle of the humerus, with displacement into the elbow joint, are reviewed by Smith<sup>901</sup> from the fracture service of the Presbyterian Hospital in New York. The ages of the 21 patients were from 7 to 17; 18 were from 9 to 14. Treatment was surgical with exposure of the joint, extraction of the medial epicondyle from the joint, reduction of the dislocation of the elbow and, finally, fixation of the epicondyle to the condylar ridge by means of a heavy silk suture passed through a drilled hole in the ridge. This procedure was used in 15 cases; in 1, a stainless steel screw was used, and in 5, the epicondyle was excised and the conjoined tendon of the flexor pronator group of muscles was sutured to the medial condyle with heavy silk. Follow-up reports in 20 of the 21 cases are given. These averaged three years. Results in 6 cases were perfect; in 4, excellent results were noted (slight prominence or irregularity of the medial epicondyle); in 9, results were good to excellent (slight limitation of elbow flexion or extension), and in 1 case, the result was fair, the epicondyle having been removed after a previous operation in another clinic. No economic loss occurred in any case. All patients with ulnar palsy recovered complete function.

In a discussion of fractures of the olecranon, Wertheimer<sup>902</sup> maintains that closed reduction is satisfactory only when there is no separation between the fragments and they are in perfect apposition. He lists indications for surgical treatment, illustrating treatment with steel wire, graft, nails and sutures. He presents 15 cases, treatment in 11 of which was by open operation. In 6 of these, cotton thread was used; in 1, heavy silk; in 2, nails, and in 1, a Moreira screw.

Hustin<sup>903</sup> reports 12 cases of fracture of the olecranon, in which he treated the fracture with the Davis lag screw. With a special screw driver and by marking the point of entrance for the screw, it was

901. Smith, F. M.: Displacement of Medial Epicondyle into Elbow Joint, *Ann. Surg.* **124**:410-425 (Aug.) 1946.

902. Wertheimer, L. G.: Fracture of Olecranon, *Rev. clín. de São Paulo* **18**:87-92 (Sept.) 1945.

903. Hustin, A.: Suture of Fractures of the Olecranon with Screws, *Mém. Acad. de chir.* **72**:261-262 (April 10-May 15) 1946.



possible to place this deep-threaded screw in the center of the cancellous bone of the ulna.

Key<sup>904</sup> presents the case of a boy of 11, seen forty-eight hours after injury, with the head of the radius displaced into the posterior part of the joint. The head was removed through a posterolateral incision and then was replaced in approximately normal position, the elbow was fixed to 90 degrees and the soft tissues were sutured around the head. The arm was immobilized for eight weeks. Thirteen months later movement of the elbow was almost normal, with 5 degrees less extension than on the other side. There was no pain and growth was satisfactory, although late roentgenograms showed an irregularity of the epiphysial plate.

*Fractures of the Forearm.*—An excellent article including the study of supination and pronation, with special reference to treatment of forearm fractures, is presented by Patrick.<sup>905</sup> The study is based on 637 cases of fractures of the forearm, from which are excluded those with imperfect reduction or malalignment. The author discusses limitation of rotation following union without displacement. He states that limitation of rotation develops in Colles' fractures, persisting for many months and sometimes becoming permanent. Patients with this type of fracture experience pain over the head of the ulna, in connection with forced supination or pronation. Most fractures of the head of the radius produce no limitation of rotation unless there is comminution or pronounced displacement, necessitating operation.

Patrick states that, since the normal range of pronation is checked by the radius crossing the ulna and compressing the deep flexor muscles between the two bones, anything encroaching on this space, such as fibrous tissue, callus or edematous tissue, will alter the compressibility of the flexor muscles and limit pronation. In all fractures of the middle third of the radius or ulna some loss of pronation occurs and persists for a considerable time after union has taken place. In isolated fractures of the ulna some degree of loss of rotation is present for a time after union, especially in fractures at the level of the attachment of the interosseous membrane. Fibrous tissue or callus rarely extends far enough to involve the radius. In isolated fractures of the radius operation causes some increase in fibrous tissue reaction around the fracture, but any further involvement of the interosseus membrane from the radial side does not affect the range of rotation.

Fractures of the shaft of the radius and ulna above the level of the interosseous membrane are rare; there are only 7 in this series,

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904. Key, J.: Survival of Head of Radius in Child After Removal and Replacement, *J. Bone & Joint Surg.* **28**:148-149 (Jan.) 1946.

905. Patrick, J.: Study of Supination and Pronation with Special Reference to Treatment of Forearm Fractures, *J. Bone & Joint Surg.* **28**:737-748 (Oct.) 1946.

in all of which union took place with minimum displacement and no loss of supination or pronation occurred once the fractures had united.

In fractures of both the radius and the ulna, limitation of rotation is due to a combination of the factors present in fractures of the radius and ulna occurring separately. The triangular fibrocartilage often escapes damage in double fractures of the forearm, so that the fractured ulna is the main cause of limitation of rotation.

Zarazoga<sup>906</sup> analyzes a series of 279 cases of fractures of the forearm in children. In the age group from 3 to 5, only the middle third of the forearm was involved. In children from 6 to 10, the fractures occurred in the middle and lower thirds of the arm, and at 12, in the middle third again. In 80 per cent the cause was indirect violence; 12 per cent of these fractures were complicated. In 20 per cent the cause was direct, one-half of these fractures being compound. Fractures of both bones occurred in 75 per cent of patients, and isolated fractures of the radius occurred in 20 per cent. Fractures of the ulna occurred in only 5 per cent, fracture of the ulna with luxation of the radius, in 3 per cent, and fracture of the radius with luxation of the ulna, in slightly less than 3 per cent. The author states that loss of rotation rarely develops in children when a reasonably good closed reduction of the fracture has been obtained.

Fractures of the forearm are discussed by Agrifoglio,<sup>907</sup> with the recommendation of the following procedure if ordinary methods of reduction should fail: manual traction for two to five minutes; reduction by pressure with the fingers, and fixation with a plaster splint, holding the forearm in pronation and the hand in pronation and dorsiflexion. Open reduction is recommended if this procedure also should fail. The author suggests using a splinter of bone from the fracture site as an intramedullary peg to hold the fragments in place and tying the fragments together with heavy catgut. Immobilization is maintained for at least six weeks. Excellent results were obtained in 5 cases.

Caceres<sup>908</sup> presents 2 cases of fracture of the bones of the forearm in young children (5 and 9), in which he used a simple expedient for reduction and retention. In the case of the child of 9, there was a fresh fracture of the radius, two fingerbreadths above the styloid apophysis. In the second case, both bones were fractured higher. The method used by the author was insertion of a Steinmann pin from the dorsal surface through the radius, using it as a lever to assist in the

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906. Zarazoga, J.: Forearm Fractures in Children, *Rev. méd. de Córdoba* 34:75-82 (Feb.) 1946.

907. Agrifoglio, M.: Bloodless Therapy and Intramedullary Pegging in Fractures of Lower Segment in Adolescents, *Arch. ortop.* 57:60-72 (Jan.) 1942.

908. Caceres, M. A.: Treatment of Forearm Fractures Difficult to Reduce and Maintain in Position, *Semana méd.* 1:248-253 (Feb. 7) 1946.

reduction of the fracture, after which a plaster cast was applied directly to the skin, with reenforcement around the pin to prevent its moving. In both cases, reduction was excellent and consolidation prompt, with perfect functional and esthetic results. The use of metallic osteosynthesis on growing bones is usually dangerous, but the author considers the procedure to be without risk. The approach is from the dorsum, to avoid important vessels and nerves.

[ED. NOTE (W. G. S.).—This procedure is much like the pin fixation in cast which was described by J. E. M. Thomson many years ago.]

Rose<sup>909</sup> describes a simple but effective device for applying traction to the wrist and forearm. It consists of two crossbars, which clamp to the table top and project about 12 inches (30 cm.) over the side. The patient's head lies on the upper one, with the upper arm parallel to the bar and about 4 inches (10 cm.) from it. The arm is attached to the bar with a band of gauze. A felt pad on the anterior aspect of the arm is for countertraction. The elbow is then bent to 90 degrees, and traction is applied to the forearm with a single loop of 3 inch (7.5 cm.) gauze bandage around the thumb. The gauze is tied to sash cord passed through a pulley attached to the lower bar, which is at the patient's feet. Two weights, up to 25 pounds (11.3 Kg.) each, are applied for thirty minutes. The device has been used by eighty to ninety surgeons at Charity Hospital in New Orleans in the reduction of over 1,500 fractures of the forearm, without a single instance of circulatory complications. The cast can be applied with the traction device in place. Traction can also be applied to the middle finger instead of to the thumb, for traction in the line of the axis of both bases. For reduction in cases of Colles' fracture, the thumb is used.

Maia<sup>910</sup> reports a group of 8 cases of Monteggia's fracture, 6 of which were in children and 2, in adults. There was one open reduction. Good results were reported in all cases. The author states the belief that open operation should be reserved for old fractures and those with involvement of the nerves.

Two cases of nonunion after the use of Kirschner pins in both bones of the forearm are reported by Guilleminet.<sup>911</sup> One was in a boy of 7. The pins were put in the day after the fracture occurred and removed in twenty-five days. The arm was kept in plaster. Three months later, there was angular deformity. The bone ends were freshened and the pins reinserted and left in for three months.

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909. Rose, R. M.: Simple Traction Device for Reduction of Forearm, *J. Bone & Joint Surg.* **28**:176-177 (Jan.) 1946.

910. Maia, B.: Monteggia Fracture, *Arq. brasil. de cir. ortop.* **12**:181-188, 1944.

911. Guilleminet, M.: Intramedullary Nailing of Both Bones of Forearm, *Lyon chir.* **40**:763-765 (Nov.-Dec.) 1945.

*Fractures of the Wrist.*—An analysis of 66 cases of fractures of the carpal scaphoid bone is presented by Bannerman.<sup>912</sup> In this series of cases, 42 per cent of the fractures of the carpal scaphoid bones were not diagnosed at the time of injury. In 35 per cent of the series, the fractures were either diagnosed as sprains and not examined roentgenographically or the roentgenogram was reported as not showing fracture and the diagnosis was missed. These factors resulted in prolonged convalescence. Complete and prolonged immobilization is the accepted treatment in all cases, even ten months after injury; satisfactory results were observed in 15 per cent more of the patients who received this treatment alone. Reduction of fractures of the carpal scaphoid bone is seldom necessary. When seen in association with dislocation of the semilunar bone, the fragments of the carpal scaphoid bone are usually in a good position after the semilunar bone has been reduced. The series contains 2 cases of this type. Immobilization by skin-tight cast, involving the thumb and extending from the elbow to the distal palmar crease, was the method used. The wrist was held in moderate dorsiflexion and slight radial deviation. The thumb was held in abduction, and extension was included to the distal phalanx. The cast was changed when it became loose, owing to atrophy of the muscles of the forearm. The atrophy was minimized by use of the fingers during immobilization. Roentgenograms taken in all positions every six weeks, and immobilization was continued until the fracture line disappeared. Inclusion of the thumb is essential for the purpose of holding the fragments in most intimate contact, and because complete immobilization cannot be accomplished unless this is done; union rarely occurs when the thumb is not included.

In 56 cases, or 85 per cent of the series, the fracture was healed without arthritic changes by prolonged immobilization. The presence of osteoporosis of the carpal scaphoid bone due to trauma was no bar to healing in the 6 cases of this condition. Immobilization was continued until complete revascularization had taken place. This was evidenced by the gradual decrease of sclerosis of the fragment and by the restoration of uniform density, as shown in roentgenograms.

Operation was not done until at least two months of immobilization had failed to show improvement. Operation was performed in 10 cases; fractures in 6 of these healed, with good results. In 2 cases with pronounced arthritic change, the distal fragment was removed; the result was good in 1. After immobilization recovery of function was surprisingly rapid in both operative and nonoperative cases. All patients regained full motion and strength after only one month of use and physical therapy.

912. Bannerman, M. M.: Sixty-Six Cases of Fracture of the Carpal Scaphoid, *Arch. Surg.* 53:164-168 (Aug.) 1946.

Fracture of the carpal scaphoid is common in military practice, and from the standpoint of time lost, persistence of symptoms and disability, the condition is comparable to fracture of the femoral neck. Disability is due to failure to recognize the fracture soon after injury, to inadequate treatment (with regard to immobilization during the period of fixation) or to disturbance of circulation to the proximal fragment, with delay in union. Sashin<sup>913</sup> saw 64 patients with such fractures from January 1943 to April 1945. Only 39 patients had undergone immobilization of the wrist in plaster soon after injury; in this group, 34 had union. Nonunion was found in 29 of the 64; 20 were operated on (methods consisted of excision of the proximal fragment or drilling or grafting of bone). Firm bony union was obtained in 4 cases; in 4 others, there was roentgenographic evidence of union, but the fracture line was visible six months after operation. In 2, there was no union after grafting of bone, so excision of the proximal fragment was done.

A lengthy, detailed roentgenographic study of the carpal scaphoid is given by Trial,<sup>914</sup> who presents a table of six positions to be used in taking roentgenograms of this fracture. The author discusses the types of fracture occurring in the scaphoid and recommends that these roentgenographic views be taken: (1) anteroposterior view with fist closed; (2) anteroposterior view with the palm to the plate; (3) front views of both hands in moderate abduction and (4) a lateral and two oblique views.

[ED. NOTE (W. G. S.).—In questionable cases these special views would be of great value.]

Bedrick and Zawadzki<sup>915</sup> emphasize that wrist injuries are rarely simple sprains and should be studied at roentgenologic examination. Fracture of the scaphoid is shown more easily by ulnar deviation of the hand than by radial deviation or anteroposterior projection. The diagnosis is usually based on the history of a fall on an outstretched hand, and the treatment for a fresh fracture is immobilization in an unpadded plaster cast for eight weeks. In doubtful cases, the injury should be treated as a fracture and roentgenograms made again in ten days. The authors state that old fractures were treated either with a bone peg or by simple drilling through and across the fracture line. The authors saw 31 fractures of the carpal scaphoid among 210 fractures of the forearm and wrist observed in thirty-six months. Bony

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913. Sashin, D.: Treatment of Fractures of the Carpal Scaphoid: Report of Sixty-Four Cases, *Arch. Surg.* **52**:445-465 (April) 1946.

914. Trial, R.: Roentgen Exploration of Carpal Scaphoid and Its Application to Diagnosis of Fractures, *Rev. corps san. mil.* **1**:504-526, 1945.

915. Bedrick, J. J., and Zawadzki, S. A.: Some Observations on the Fractured Carpal Scaphoid, *Mil. Surgeon* **98**:488-491 (June) 1946.

union occurred in 95 per cent of the cases of fresh fracture treated by immobilization in a skin-tight cast.

Macrossan<sup>916</sup> presents reports of 3 cases of sprain, with and without "flake" fracture of the carpal scaphoid, in boys of 11 and 12. The sprains occurred at the attachment of the radial collateral ligament of the wrist joint to the scaphoid. The violence producing them was forcible ulnar deviation, accompanied by palmar flexion or dorsiflexion at the wrist. The maximal point of tenderness was in front, over the tuberosity of the scaphoid, in what appeared to be a minor strain of the wrist. Roentgenograms may show partial separation of a discrete flake of bone or evidence of a lesser degree of damage to the scaphoid at the attachment of the radial collateral ligament. Fixation in plaster is necessary when symptoms persist beyond a week or two.

*Fractures of the Hand.*—Acute injuries of the first metacarpal bone in military personnel are discussed by Van Demark.<sup>917</sup> In cases of Bennett's fracture combined with dislocation of the thumb, when manipulative reduction is not successful, the treatment of choice is skeletal traction, applied through the distal part of the first metacarpal bone or the proximal phalanx and combined with immobilization in plaster of paris in the position of function. The cast should cover the forearm and be closely molded laterally at the base of the thumb, and in the palm it should extend to the level of the necks of the metacarpal bones, permitting full motion of the fingers. Fracture of the shaft and base of the first metacarpal bone usually occurs at or near the junction of the shaft with the base. The distal fragment is angulated medially by the thenar and the long flexor muscles of the thumb, the proximal fragment being held in abducted position by the long abductor muscle. After reduction and immobilization in plaster frequent roentgenologic examination is done. With proper care an almost perfect anatomic result can be obtained. A similar brief discussion of sprains and subluxations of the adjacent joints and of dislocation of the first metacarpophalangeal joint is included in this report. In cases of dislocation of the first metacarpophalangeal joint, closed reduction is usually possible and should be followed with a four week period of immobilization in flexion, to prevent recurrence.

Twenty cases of fractures of the shaft of the metacarpal bones were treated by Barba Inclán<sup>918</sup> after the method of Berkman and Miller, in which one or two Kirschner pins are introduced from the side of

916. Macrossan, K. I.: Sprain Fracture of the Carpal Scaphoid in Children, *Lancet* 1:341-342 (March) 1946.

917. Van Demark, R. E.: Acute Injuries of First Metacarpal in Military Personnel, *Mil. Surgeon* 99:127-130 (Aug.) 1946.

918. Barba Inclán, A.: Internal Fixation in Therapy of Fractures of the Last Four Metacarpals, *Bol. Sec. san. policia nac.* 1:62-65 (April-June) 1945.

the hand nearest the fractured metacarpal bone. The first metacarpal bone is excluded from this treatment, and the author also makes an exception in cases of avulsion of the styloid process of the third metacarpal bone, for which he recommends open operation and direct suture.

The mechanism of metacarpophalangeal luxations of the thumb is discussed in an article by Giordanengo.<sup>919</sup> The author describes three types of luxation and discusses the differential diagnosis of this condition when it is complicated by fracture of the distal end of the metacarpal bone or the proximal end of the phalange. Maneuvers for reduction are described.

The treatment of fracture-dislocation of the interphalangeal joints of the hand is discussed by Robertson and Cawley.<sup>920</sup> The injury occurred in 7 cases recorded in a large Army general hospital in one year, as a result of baseball injuries. The injury was due to a blow on the end of an extended finger, which produced a small, palmar fragment, retracted proximally by the capsule. Treatment was with three Kirschner wires connected to a wire extension, the first transversely through the neck of the proximal phalanx, the second transversely through the base of the phalanx distal to the dislocation and the third transversely through the neck of the phalanx. With rubber bands, traction was obtained on these wires to reduce and hold the fracture. In all 7 cases, reduction was well maintained, bony union of the fragment was obtained and function was excellent.

Curry<sup>921</sup> stresses the importance of painstaking care in industrial injuries of the fingers. Roentgenologic examination of all suspected fractures, before and after reduction, is important. The author outlines the methods of treatment for fractures involving the distal phalanx, the middle phalanx, the proximal phalanx and the thumb, indicating the insertions of tendons which produce different deformities and the type of flexion or extension which will overcome such deformities. The underlying principle in treatment of all fractures of the finger is the matching of the mobile distal segment to the less mobile proximal segment. Disturbance of the circulation must be prevented. In the section on amputations the author emphasizes the importance of saving as much of the finger as possible, as reparative processes are complicated. The loss of soft parts, continuous pain from permanently damaged nerves, complete loss of tendons and fixation of a joint, with

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919. Giordanengo, G.: Dislocations of the Metacarpophalangeal Luxations of the Thumb, *Minerva chir.* 1:92-94 (May) 1946.

920. Robertson, R. C.; Cawley, J. J., Jr., and Faris, A. M.: Treatment of Fracture Dislocation of Interphalangeal Joints of Hand, *J. Bone & Joint Surg.* 28:68-70 (Jan.) 1946.

921. Curry, G. J.: Treatment of Simple and Compound Finger Fractures, *Am. J. Surg.* 71:80-83 (Jan.) 1946.

deformity, are among the indications for amputation. Sites that are best for amputation are listed.

A method of reducing fracture-dislocations of the proximal interphalangeal joints of the fingers is described by Schulze.<sup>922</sup> The procedure consists of placing the joint in extreme flexion while producing traction on the finger, thus reducing both the fracture and the subluxation. In most cases, no pressure is required to maintain reduction as long as the position of acute flexion is not allowed to lapse. The position can be maintained with a strip of adhesive tape placed around the flexed finger. If the finger is short and thick or if swelling interferes with full flexion it may be desirable to use a splint made of a strip of aluminum. Because of the pain and the immediate, pronounced deformity, these injuries are usually seen early, at which time swelling is generally not great and reduction is accomplished with little pain. In a week or ten days, the finger is gradually extended, while immobilization of the joint and protective splinting are continued.

#### FRACTURES OF THE LOWER EXTREMITY

*Fractures and Dislocations About the Hip Joint.*—Feldman<sup>923</sup> states that gunshot wounds of the hip were the gravest injuries of the extremities observed during the war. These wounds were often accompanied with severe complications, giving rise to high mortality and to invalidism. Sepsis with anaerobic infection was the main cause of death among patients returned to hospitals in the rear. The author states the belief that results depend fundamentally on the length of time before removal from the battlefield, on the quality and time of surgical treatment and on immobilization. He recommends careful surgical treatment under complete anesthesia and advises immediate amputation when virulent gaseous infection is present. The need to prevent complications by cleanliness of the wound, careful surgical treatment, blood transfusions and massive intravenous doses of sulfanilamide is stressed. The author recommends concentration in one army hospital of all patients with grave injuries to the extremities, particularly those with hip injuries.

Alcivar-Elizalde<sup>924</sup> discusses 2 cases of fracture of the femoral shaft with dislocation of the hip in the newborn, caused by forcible maneuvers during delivery. The clinical picture in each case was characteristic, showing disproportion in the length of the infant's limbs, with pain

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922. Schulze, H. A.: Treatment of Fracture-Dislocations of Proximal Interphalangeal Joints of Fingers, *Mil. Surgeon* 99:190-191 (Sept.) 1946.

923. Feldman, K. I.: Therapy of Gunshot Wounds of Hip, *Khirurgiya*, 1945, no. 3, pp. 55-63.

924. Alcivar-Elizalde, E.: Obstetric Dislocation of Hip Associated with Fracture of Femur, *J. Bone & Joint Surg.* 28:838-841 (Oct.) 1946.



on motion, followed in two to three days by swelling in the inguinal, thigh and gluteal regions. The prognosis was favorable when treatment was started during the first fifteen days after birth. The author used the Lorenz procedure, employed for congenital dislocations, and ether anesthesia. The normal hip was fixed while the operator flexed the injured thigh on the abdomen, with the hip and knee flexed. The extremity was then rotated externally. This maneuver was sufficient to produce reduction, which was checked by roentgenograms. Immobilization, with the limb in 135 degrees flexion, 40 degrees abduction and slight internal rotation, was maintained for forty-five days in a castex® or plaster spica. The results in these 2 cases were good, as shown by roentgenograms and by the efficiency of the limb, the infants having learned to walk at 14 or 15 months, with normal gait and development.

[ED. NOTE (W. G. S.).—These injuries were complete dislocations with incomplete fractures, which explains the author's success with manipulative reduction.]

Quist-Hansen<sup>925</sup> reports that 10 traumatic dislocations of the hip joint comprised 8.5 per cent of all dislocations observed at the Municipal Hospital in Bergen, Norway, during the period from 1927 to 1941. He states that laceration of the ligamentum teres and lesion of the capsule in a traumatic dislocation lead to a greater risk of ischemia of the femoral head in children and adolescents than is the case in full-grown persons. The author presents a case of necrosis of the femoral head, the condition having occurred after traumatic dislocation of the hip joint in a boy of 4. The patient was observed for a period of two and a half years. A control examination of 8 other patients with traumatic dislocation of the hip joint, of which 3 were under 10, revealed no signs or symptoms of necrosis of the head two and three quarters to ten and a half years after injury. The author recalls that experiments on animals by Muller, in 1924, demonstrated the high frequency of necrosis during the period of growth. A comparison of age distribution in 370 cases of traumatic dislocation of the hip joint and in 49 cases of necrosis of the femoral head after this injury shows that in human beings the risk of necrosis of the head is great during the period of growth, with a rapid drop in frequency after the closing of the epiphysial line at the age of 18 to 20.

Sabate<sup>926</sup> gives a detailed case history of a man of 20, who at the age of 13 had experienced an ischiatic type of coxofemoral dislocation due to a fall; the dislocation was reduced, and the hip functioned

925. Quist-Hansen, S.: Caput Necrosis After Traumatic Dislocation of the Hip Joint in Four Year Old Boy: Control Examinations of Eight Cases of Luxatio Coxae Traumatica, *Acta chir. Scandinav.* **92**:393-402, 1945.

926. Sabate, S. J.: Necrosis of the Head of the Femur Following Ischiatic Variety of Coxo-Femoral Luxation, *Med. clin., Barcelona* **6**:171-176 (March) 1946.

normally for seven months. A second fall then produced pain in the hip, which was violently manipulated once weekly for a month, after which relaxation of the femoral head was followed by claudication and pain, which lasted for months. There was gradual improvement, and when the author again saw the patient at the age of 20, there was little outward evidence of the condition of the hip. The author includes a lengthy analysis of the pathologic conditions in this case of aseptic necrosis, followed by a lengthy discussion of the causes and measures for preventing such disturbances.

*Intertrochanteric Fractures.*—O'Brien, Shy and Bubliss<sup>927</sup> report on 103 consecutive cases in which trochanteric fractures were treated by internal fixation. Spinal anesthesia was used in 29 cases, with 4 deaths (13.8 per cent); ether drop method in 10, with 2 deaths (20 per cent); thiopental sodium (pentothal sodium®) and nitrous oxide anesthesia in 34, with 3 deaths (8.8 per cent), and local anesthesia in 30, with 13 deaths (43.4 per cent), a total of 22 deaths (21.4 per cent) from anesthesia. The average age of the patients was 70.6, including persons up to 89. The operative technic for reduction and insertion of the blade plate is described in detail, as is the postoperative care. The result of a one to two and a half year follow-up of 50 of the 81 survivors were: 20 (40 per cent), excellent; 11 (22 per cent), good; 8 (16 per cent), fair, and 11 (22 per cent), poor.

Briggs and Keats<sup>928</sup> recommend skeletal traction with beaded Kirschner wires for treating intertrochanteric fractures of the femur. The authors consider the advantages of this method to be ease in nursing care, early mobilization of the knee and almost perfect anatomic reduction; they treated 18 of 32 patients in this way, with good functional and excellent anatomic results in 16. The method of application is described.

*Fractures of the Neck of the Femur.*—Numerous articles were published on this subject in 1946, but no radical changes or new ideas were presented.

Menegaux and Lescaux<sup>929</sup> illustrate the current trend away from the use of guides. Theirs is an illustrative comment that the numbers of new directional guides presented yearly for nailing fractures of the femur would make one think that this operation has only one

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927. O'Brien, R. M.; Shy, J. C., and Bubliss, N. J.: Internal Fixation of Trochanteric Fractures of Femur: Report of One Hundred and Three Consecutive Cases, *J. Bone & Joint Surg.* **28**:791-797 (Oct.) 1946.

928. Briggs, H., and Keats, S.: Management of Intertrochanteric Fractures of the Femur by Skeletal Traction with Beaded Kirschner Wire, *Am. J. Surg.* **71**:788-796 (June) 1946.

929. Menegaux, G., and Lescaux, B.: Nailing of Fractures of the Femoral Neck Without Directional Apparatus, *Mém. Acad. de chir.* **71**:368-373 (Oct. 17-31) 1945.

delicate stage (the placing of the guide) which is all-important to the success of the nailing. The authors dispensed with the guide in the last 17 of the 50 cases reported; the importance of perfect reduction with adequate roentgenographic control is stressed as being of more significance than the use of guides for aiming a nail.

Chaton<sup>930</sup> also recommends simplification of the technic for nailing of fractures of this type and suggests preliminary reduction and immobilization in plaster before moving the patient to the operating room, where operation is performed through a windowed cast.

[ED. NOTE (W. G. S.).—This method would perhaps simplify the technic in small hospitals where no fracture table is available, but otherwise it would seem to be superfluous.]

Pelissier<sup>931</sup> presents his aiming apparatus, which is an adaptation combining the best features of the Bopp goniograph and the Merle d'Aubigne apparatus.

DoAmaral<sup>932</sup> presents a lengthy thesis, with a detailed anatomic study, classification of fractures and a discussion of relative frequency, symptoms, roentgenographic diagnosis and treatment. He reviews 9 cases in which fractures were treated by Whitman reduction; 5, with the Albee bone peg; 6, with Smith-Petersen nailings and 24, with the Godoy Morlira screw. He reported osseous union in 21 and pseudarthrosis in 3 cases in the last group.

Speed<sup>933</sup> lists the errors of omission and of commission usually responsible for failure in the surgical treatment of fractures of the hip and stresses the need for frequent roentgenologic checking during and after fixation, for the proper angle of insertion of nails or pins, for proper support for the fracture and the avoidance of too early weight bearing. The author considers bone grafts in addition to nails or pins to be of insufficient value for the added trouble and time required. For nonunion he recommends subtrochanteric osteotomy as giving better results than attempts at reduction and pin fixation.

Barba Inclán<sup>934</sup> describes his method of treatment in stages. The first is reduction under local anesthesia, with insertion of a Stader

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930. Chaton, M.: Attempted Simplification of Technic of Nailing Fractures of the Femoral Neck, *Mém. Acad. de chir.* **71**:488-491 (Nov. 28-Dec. 19) 1945.

931. Pelissier, G.: The Purpose of Nailing of Fractures of the Femoral Neck: Presentation of an Aiming Apparatus, *J. de radiol. et d'électrol.* **27**:255-256, 1946.

932. doAmaral, A. C.: Therapy of Fractures of the Femur by Brazilian Method of Godoy Moreira (Extra-Articular Fixation), *Rev. méd. munic.* **6**:245-295 (March-April); 478-532 (May-June) 1946.

933. Speed, K.: Treatment of Fractures of the Hip: Surgical Technic, *S. Clin. North America* **26**:230-248 (Feb.) 1946.

934. Barba Inclán, A. B.: Surgical Therapy of Fractures of the Neck of the Femur by Bone Graft in Several Stages, *Cir. ortop. y traumatol., Habana* **12**:106-114 (July-Sept.) 1945.

nail in the lower third of the femur for maintenance of the position in a plaster spica. The second stage, which is carried out one week after the reduction, is removal of a cortical graft from the tibia of either the patient or a bone donor. The graft is kept in citrated blood, under refrigeration, for one week. The third stage, performed after another week, consists of insertion of the bone graft. A large window is cut in the spica over the trochanteric region, and with the aid of the author's guide and a roentgenographic check the previously modeled graft is inserted in a drilled hole. Use of the spica is continued after operation for seventy to eighty days, and walking with crutches is begun in one hundred days.

Therkelsen<sup>935</sup> describes an extracapsular method for removal of the central fragment of a broken steel nail: A thread is cut in the central fragment and a screw inserted, which can be used as a handle for removal.

Joensen<sup>936</sup> and Branes<sup>937</sup> each report a case of spontaneous fracture of the femoral neck following roentgen irradiation and radium therapy for cancer of the cervix. Both fractures occurred two years after roentgen therapy was first given. Joensen collected from the literature reports of 25 cases of spontaneous fracture of the femoral neck following roentgen irradiation; the fractures were bilateral in 2 cases. In 1 case ankylosis of the hip resulted from irradiation without evidence of a fracture.

Pennis,<sup>938</sup> in a study of the end-results of fractures of the femoral neck, reports on 254 cases from the files of the state insurance fund of the Netherlands. Most of the patients were men, the exact number being 228 men and 26 women. The average age was 49.7; only 4 patients were over 69, and 12 were under 40. The results were good in 163 cases, satisfactory in 18, unsatisfactory in 56 and unknown or questionable in 17; results were thus good or satisfactory in nearly 70 per cent of the cases. The data on type of therapy are vague, which is not surprising in view of the source of the material and the author's purpose in studying this particular type of statistics.

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935. Therkelsen, F.: Extracapsular Removal of Broken Steel Nail Used in Osteosynthesis of Femoral Neck, *Nord. med. (Hospitalstid.)* **15**:2301-2302 (Aug. 15) 1942.

936. Joensen, H. D.: Spontaneous Fracture of the Femoral Neck Following Roentgen Irradiation, *Nord med. (Hospitalstid.)* **12**:3718-3720 (Dec.) 1941.

937. Branes, J. F.: Fractures of the Femoral Neck Following Roentgen and Radium Therapy of Cancer of the Uterine Cervix: Case, *Arch. Soc. cirujanos hosp.* **15**:589-591 (June) 1945.

938. Pennis, P. W. L.: Therapeutic Results of Fractures of the Femoral Neck According to Data of State Insurance Fund, *Nederl. tijdschr. v. geneesk.* **90**:147-149 (Feb. 16-22) 1946.

[ED. NOTE (W. G. S.).—Obviously a series of cases in this group of young persons, composed mostly of men, would yield a higher percentage of satisfactory results than is usually reported. However, I feel that the author's outlook is a little optimistic, even considering the unusual source of material.]

Leira<sup>939</sup> reports the end-results in 103 cases of fracture of the femoral neck, observed from 1933 to 1941 in the Trondheim Hospital in Norway. Thirty-nine patients were treated by traction, reduction or bed rest, or with plaster casts; 64 were treated with the Smith-Petersen-Johansson nail. The minimum period of observation was two years. In both groups women predominated; results were far better in the case of men. In the nonsurgically treated group more than half the patients showed displacement of the fracture site and 6 had necrosis of the head of the femur. Two failures were considered due to initial trauma, 2 secondary to pseudarthrosis and 2 secondary to early weight bearing. In the surgically treated group, in which 64 fractures were nailed, satisfactory results were recorded in 32 cases, good results in 2 and unsatisfactory results in 30; osseous union occurred in 87.5 per cent. The unsatisfactory results were ascribed to aseptic necrosis in 17 cases, to pseudarthrosis in 8 (12.5 per cent) and to arthritis deformans in 22 (45 per cent). In conclusion, the author states emphatically that the patient should be kept in bed until osseous healing of the fracture occurs.

Harstad and Paulsen<sup>940</sup> studied 112 cases of fractures of the femoral neck treated by nailing. Reexamination was made one to six years after initial treatment; in 84 cases examination was roentgenographic, and in 28 clinical. Results in 60 per cent of the cases were considered satisfactory. Pseudarthrosis was present in 16 cases and aseptic necrosis in 13. Unsatisfactory reduction and unsatisfactory position of the nail were considered the chief causes of pseudarthrosis. Aseptic necrosis seemed to be almost inevitable, since it occurred in cases in which the patients showed good reduction and osseous union. The authors state that the nail is of no importance as a causative agent for aseptic necrosis.

Heide-Jørgensen and Schondel<sup>941</sup> report the cases of 58 patients, 47 with fractures of the femoral neck and 11 with pertrochanteric fracture; 30 were 70 at the time of treatment. All were treated surgically,

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939. Leira, H.: Results of Treatment of Fractures of the Femoral Neck in Trondheim Hospital from 1933 to 1941, *Nord. med.* **31**:2084-2094 (Sept. 13) 1946.

940. Harstad, K., and Paulsen, K.: Examination of Nailed Fractures of the Femoral Neck, *Nord. med. (Norsk mag. f. lægevidensk.)* **27**:1571-1574 (Aug. 10) 1943.

941. Heide-Jørgensen, H., and Schondel, C.: Surgical Therapy of Fracture of Femoral Neck and of Pertrochanteric Fractures with After-Examination of Operated Patients, *Nord. med. (Hospitalstid.)* **17**:329-331 (Feb. 27) 1943.

the mortality rate being 10 per cent in the cases of fracture of the femoral neck and 9 per cent in those of pertrochanteric fracture. At the end of one year 33 patients were examined, and the results were summarized as follows: excellent, 26 cases; satisfactory, 4; poor, 2, and no opinion, 1. In 4 cases another operation was performed and the fracture nailed again; removal of the nail was done in 7 cases. Bony union occurred in 29 cases, the outcome was uncertain in 1 and unjudged in another and 2 patients had necrosis of the femoral head.

*Fractures of the Shaft of the Femur.*—McKeever,<sup>942</sup> on the basis of a study of 47 cases of closed fracture of the femur, in all of which the patient, though originally treated by different army surgeons, ultimately came under the author's care, makes recommendations about the promiscuous use by average surgeons of procedures requiring high skill and special armamentarium. Among the 47 patients, 23 had been treated by some form of suspension; 17 had had open reduction and metallic plate fixation and/or screw fixation (10 primary and 7 secondary), and 7 had had external skeletal fixation. The shortest periods of absolute recumbency were seventy days for external skeletal fixation, seventy-seven for internal fixation and ninety for traction. The longest periods were three hundred and sixty-five days for internal fixation, three hundred and twenty-six for external skeletal fixation and one hundred and ninety-three for traction. The author studied other phases, such as protection, the time required for roentgenographic evidence of bony union, the status of the joints, shortening, muscular atrophy and complications, concluding that the safest method for the average surgeon in the average hospital is traction. Under average circumstances open reduction should be reserved for patients showing well founded evidence of soft tissue interposition after a trial of treatment by traction. The general use of apparatus designed for skeletal fixation and ambulation is likely to delay union and carries a great risk of producing osteomyelitis at the sites of fixation pins.

Lusskin and Hoffman<sup>943</sup> discuss the limitations in the treatment of fractures aboard a hospital ship and recommend plaster spica casts with full and half pin fixations. No follow up of the cases is presented.

Hart<sup>944</sup> comments on stiffness of the knee, which he considers the major complication in cases of fracture of the femur. He discusses in great detail a program for the restoration of function through active, objective, resisted and non-weight-bearing exercises.

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942. McKeever, F. M.: Treatment of Fractures of Shaft of Femur, Bull. U. S. Army M. Dept. 5:690-696 (June) 1946.

943. Lusskin, H., and Hoffman, R. R.: Fractures of Shaft of Femur: Early Treatment on Hospital Ship, U. S. Nav. M. Bull. 46:888-894 (June) 1946.

944. Hart, V. L.: Balanced Suspension and Treatment of Fractures of the Femur, Bull. U. S. Army M. Dept. 5:57-63 (Jan.) 1946.

Allende and Malvarez<sup>945</sup> present 7 cases of traumatic separation of the lower end of the femur, all in boys 7 to 17. In 1 case there was bilateral separation of the epiphysis, and in another the separation was complicated by a fracture of the shaft of the opposite femur. In 2 cases rupture of the popliteal artery produced gangrene of the foot, requiring amputation; the Gritti type of amputation was done in each case. One patient, seen twenty-three days after injury, was treated by removal of the epiphyseal fragment and ankylosis of the knee in extension. The authors recommend reduction in flexion for twenty days and 90 degree flexion for another twenty days, followed with continuous traction to extend the knee. When the displacement was backward skeletal traction for eight to fifteen days was followed by immobilization in plaster, with the knee extended.

*Fractures of the Patella.*—Two slightly contradictory reports appeared in 1946 on patellectomy as the treatment for fractures of the patella.

Brooke<sup>946</sup> reports on 54 cases, with a follow-up study in 35, in which all patients had undergone excision of the patella five to fifteen years previously. Nineteen had sustained comminuted fractures and 16 transverse fractures, with varying degrees of separation of the fragments. Twenty-five were male and 10 female patients. The average age at the time of operation was 40. All patients returned to work in three to eight weeks after the operation. There were no osteoarthritic changes in any of those examined. In 27 cases function of the affected limb was normal in every respect; in 10 there was some disability, for varying reasons. The author stresses the use of nonabsorbable suture material, preferably linen, and prevention of insufficiency in the quadriceps.

MacAusland,<sup>947</sup> on the other hand, after reviewing the history of patellectomy, including Brooke's several articles reporting strikingly good results, mentions that the indications for the use of patellectomy in the treatment of fractures are still not clearly defined. He lists the advantages and disadvantages of patellectomy but states the opinion that patellectomy should at present be limited to cases of severely comminuted fresh fracture and of malunion after transverse fracture. He discusses operative technic, postoperative care and regeneration of the patella and gives an analysis of cases and results in 11 of his own 14 cases. Ten of the 11 patients obtained good, functional knees, with

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945. Allende, G., and Malvarez, O.: Separation of the Epiphysis of the Lower End of the Femur, *Prensa méd. argent.* **33**:495-506 (March 8) 1946.

946. Brooke, R.: Fractured Patella: Analysis of Fifty-Four Cases Treated by Excision, *Brit. M. J.* **1**:231-233 (Feb. 16) 1946.

947. MacAusland, W. R.: Total Excision of Patella for Fracture: Report of Fourteen Cases, *Am. J. Surg.* **72**:510-516 (Oct.) 1946.

perfect motion of the joint and stability. In 4 cases there was slight atrophy of the quadriceps, with loss of 10 degrees of complete extension, but the patients were asymptomatic. Five patients had normal power and motion. One patient had only 90 degrees of motion, with tenderness at the level of the joint, and the remaining patient, although clinically normal, complained of the inconvenience of going up stairs one step at a time.

*Fractures into the Knee Joint.*—Vergara<sup>948</sup> reports on 20 cases of fracture of the tibial condyle, recorded in the Instituto Traumotológico, Santiago, Chile. In 13 one tuberosity was fractured, and in 7 both tuberosities. Only 1 case was treated surgically, because of an intra-articular fragment, and although there was good function at first, the residual deformity resulted in 30 per cent disability. The author states that the spongy character of the condyle is a contraindication for surgical repair as well as an indication for complete immobilization of sufficient time to permit complete consolidation. In cases of fracture with no displacement he recommends a simple knee cast for one month; in those cases with lateral displacement, compression with clamps under spinal anesthesia, followed by use of a plaster cast for one to one and a half months, and for downward displacement, skeletal traction for four to six weeks.

Cobey<sup>949</sup> recommends a vitallium lag screw of the Lippmann type, with a large oval washer and spur, for accurate reduction and fixation of fractures of the tibial plateau. He describes the screw in detail, the method of open reduction and an application of the lag screw and washer and presents 4 illustrative cases.

Peneiro Sorondo and Ferre<sup>950</sup> discuss the open treatment of fractures of the lateral condyle of the tibia. The illustrations show the stages of the operation for removal of the meniscus between the fragments; the authors operated in 8 such cases in two and a half years. They used two Finochietto pins, long screws and wires for retention in cases of slight displacement, but state that these pins will not prevent lateral spread. They state the belief that a bolt with two nuts is best for retention of lateral spread, and that closed methods of reduction are inadequate because they do not remove the interposed meniscuses and ligaments.

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948. Vergara, G.: Therapy of Fractures of the Tibial Tuberosity, Arch. Soc. cirujanos hosp. **15**:764-770 (Dec.) 1945.

949. Cobey, M. C.: Lag Screw Fixation in Fractures of Tibial Tuberosity, J. Bone & Joint Surg. **28**:273-276 (April) 1946.

950. Peneiro Sorondo, J., and Ferre, R. L.: Fractures of the External Tibial Tuberosity, Rev. Asoc. méd. argent. **59**:1057-1061 (Sept. 15) 1945.



*Fractures of the Shaft of the Tibia and Fibula.*—Brumback<sup>951</sup> reviews the records of soldiers with fractures of the tibial shaft in an Army general hospital within the United States. Excluding patients with fractures of the tibial plateau and the malleolar region there were 120 cases, 68 of simple fracture and 52 of compound fracture. The fracture was in the upper third of the shaft in 23, in the middle third in 23 and in the lower third in 74. The results, as listed in the records, were as follows: 75 per cent of patients with simple fractures were returned to duty, 9 per cent were discharged due to disability and 11 per cent were otherwise dealt with (usually transferred nearer home); 46 per cent of patients with compound fractures were returned to duty, 31 per cent were discharged due to disability and 23 per cent were dealt with otherwise. In the entire group, 26 soldiers required operation, 10 on simple fractures (3 of these patients returned to duty) and 16 on compound fractures (10 patients returned to duty). Discharge due to disability did not indicate an unproductive civilian life.

Milgram<sup>952</sup> offers definite procedures for the open reduction of fractures of the tibial condyles and for after-treatment. He states that fractures of the tibial shaft usually have plural lines of fracture which are demonstrable later, during decalcification, and are associated with vascular damage in the bone, which affects the healing. He recommends open reduction of spiral fractures of the tibial shaft, with screw fixation, followed by exercises of quadriceps and toes while in plaster. In discussing cases of fracture of the ankle, he stresses accurate reduction and early operation for those fractures which cannot be reduced by manual attempts. He states that prolonged immobilization and non-weight-bearing for five to six months resulted in revascularization of early aseptic necrosis of the body of the astragalus in 4 cases. He discusses early diagnosis of sprain fractures of the ankle with the use of an injection of procaine hydrochloride into the hematoma and with roentgenograms, taken with inversion of the foot.

[ED. NOTE.—This method of diagnosis should not be neglected in the examination of injuries of the ankle.]

Beluffi<sup>953</sup> presents a personal case of isolated traumatic luxation of the fibula. He reviews the literature, noting that luxation of the fibula is rather common in conjunction with fracture of the fibula or tibia or both, but rare in isolation. He found only 22 cases reported since 1900, including his own; in 18 of these the diagnosis was not confirmed

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951. Brumback, J. E., Jr.: Mean Disposition of Tibial Shaft Fractures, *Am. J. Surg.* **71**:532-533 (April) 1946.

952. Milgram, J. E.: Closed Fractures of Leg and Ankle, *Bull. U. S. Army M. Dept.* **5**:727-731 (June) 1946.

953. Beluffi, E. L.: Isolated Traumatic Luxations of the Fibula, *Gior. ital. chir.* **2**:157-169 (April) 1946.

roentgenographically. Luxation of the lower end of the fibula was reported once and double luxation (both ends) once, while the remaining 20 cases, including the author's were of luxation of the upper end. The cause of this type of fracture is usually indirect, the condition rarely being directly due to sudden muscular contraction. The diagnosis is easy by roentgenologic examination, and reduction is easy by manipulation. The prognosis is excellent anatomically and functionally.

*Malleolar Fractures.*—Wilner<sup>954</sup> presents a detailed account, illustrated with drawings and roentgenograms, of the pseudofractures and true fractures that occur commonly in the bones of the ankle and foot. Stress is laid on differentiation between fracture lines and epiphysial lines, on post-traumatic ossification and periartritic deposits at the distal end of the tibia and fibula and on calcification of veins and arteries.

Hendelberg<sup>955</sup> studied fresh malleolar fractures by fluoroscopy and arthrography on cadavers and live subjects and obtained valuable data on the origin of malleolar fractures, the extent of injury to ligaments and the effects of different manipulations. The results of arthrographic studies correspond well to those of fluoroscopic examination with regard to injuries of the ligaments if done in the first twenty-four hours after fracture. Experiments on cadavers showed that even considerable widening of the anterior part of the tibiofibular mortise does not visualize in roentgenograms and that views in two routine planes do not give a complete picture of the size of the posterior tibial fragment. Thin fragments of the cortical margin, removed with a chisel, were not visualized. Fragments which appeared in roentgenograms as such included varying expanses of articular surface, often very large. The author recommends making it a rule to take a view from the back laterally, to visualize the course of fracture lines in the medial and lateral part of the joint.

O'Donoghue<sup>956</sup> makes a plea for recognition of the fact that open reduction and fixation are necessary in the treatment of fracture of the malleolus when the force has torn the malleolus away from the attachment and carried a strip of fascia into the intervening space, making nonunion certain, or when the spreading of the mortise will result in a permanently weak joint and permanent disability. The author recommends oblique roentgenographic views to reveal separation of the fragments with soft tissue interposition.

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954. Wilner, D.: Diagnostic Problems in Fractures of Foot and Ankle, *Am. J. Roentgenol.* **55**:594-616 (May) 1946.

955. Hendelberg, T.: Roentgenographic Examination of Ankle Joint in Malleolar Fractures, *Acta radiol.* **27**:23-42 (Jan. 31) 1946.

956. O'Donoghue, D. H.: Consideration of Certain Fractures of the Ankle, *South. M. J.* **39**:367-371 (May) 1946.

Thomassen<sup>957</sup> discusses Niels Hansen's work on fractures of the ankle, with classification according to the position of the foot at the moment of injury, and attempts to clarify certain misunderstandings. Hansen classified fractures in four groups: those which occur with the foot in supination, those with the foot in pronation, those due to external rotation with the foot in supination and those due to external rotation with the foot in pronation. The etiologic diagnosis may be based on the injury to the fibula or to the lateral malleolus, as revealed by roentgenograms. Fractures occurring with the foot in supination show a transverse fracture line in the lateral malleolus; fractures occurring with the foot in pronation show a fracture line directed laterally upward just above the lateral malleolus, sometimes with a small triangular lateral fragment; those due to external rotation with the foot in supination show a long, spiral fracture line running in an upward and backward direction in and above the lateral malleolus, and those due to external rotation with the foot in pronation show a fracture high on the fibula and rupture of the syndesmosis (the interosseous tibiofibular ligament). An unusual and rare type of fracture, presumably produced by exaggerated dorsiflexion of the pronated foot, causes detachment of the medial malleolus and of a large anteromedian fragment on the articular surface of the tibia. Lateral fractures of the anterior and posterior margins of the tibia are caused primarily by tearing of the anterior and posterior ligaments of the lateral malleolus. The technic for reduction, which Hansen worked out on cadavers for each type of fracture, is described, as are the criteria for determining complete reduction. It is important to draw the lateral malleolus forward so that its anterior edge is flush with, or in front of, the anterior margin of the body of the fibula if one is to succeed in closing the anterolateral tibial lesion. The prime rule is to reduce all fractures as though they were of the most severe type. On the basis of etiologic diagnosis, the author states that Hansen's manipulations make possible a reduction of even the most difficult fractures of the ankle. He refers to Hansen's book for results, and, on the basis of these and his own experience, he concludes that Hansen's etiologic diagnosis and reduction technic are of essential importance in the treatment of fractures of the ankle.

Magnusson<sup>958</sup> describes the anatomy of the distal tibiofibular syndesmosis and lists the etiologic classification of malleolar fractures caused by indirect violence (pronation, supination and external rota-

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957. Thomassen, E.: Fracture of Ankle; Etiologic Diagnosis and Reposition According to Niels Hansen: Critical Review, *Nord. med. (Hospitalstid.)* **25**:689-695 (March 29) 1945.

958. Magnusson, R.: Injuries of Distal Tibio-Fibular Syndesmosis in Malleolar Fractures, *Nord. med. (Hygiea)* **26**:1245-1250 (June 15) 1945.

tion). The author made a critical study of the common roentgenologic methods of diagnosing injuries to the tibiofibular syndesmosis. Roentgenologic evidence of injuries to the tibiofibular ligament was present in 412 cases of malleolar fracture in which operation was not performed. Such injury was also present in some cases of fractures of both malleoli due to supination. It should be noted that fractures of the internal malleolus due to pronation were accompanied with injuries to the tibiofibular ligament, which were not evident in roentgenograms until after treatment. The injuries appeared as a change in the lateral contour of the anterior tibial tubercle or in the form of a fragment torn from the anterior tibial tubercle. The author recommends the use of Hansen's etiologic diagnosis as the best way to determine the presence or absence of injury to the syndesmosis. He states that an injury to the syndesmosis is always present in fractures due to external rotation, in fractures due to pronation and in fractures of both malleoli due to supination with medial displacement of the ankle joint. The author stresses the importance of bearing in mind the possibility of injury to the syndesmosis when treating a malleolar fracture, so that diastasis in the malleolar fork may be prevented.

*Fractures of the Foot.*—Stepanov<sup>959</sup> studied in detail 104 cases of injuries of the lower extremity produced by land mine explosions and classified them into three groups, in which the incidence was as follows: closed injuries of the lower limb and foot, 54 cases (52 per cent); open wounds with multiple injuries to the bones of the foot, 24 cases (23 per cent), and ruptures of the foot and leg, 26 cases (25 per cent). The victim was standing when hit in 92 per cent of cases and crawling in 8 per cent. In 16 cases, the roentgenograms showed injuries of the calcaneus 12 times, of the metatarsal bones 11 times, of the astragalus 9 times, of the tarsal bones 5 times and of the phalanges 2 times. In 22 cases of open injuries, primary amputation was done in 2, infection occurred in 17 (resulting in amputation of the leg in 4, in 1 of which the patient died), improvement was noted under treatment in 6 and amputation was done later in 7. Thus, in 22 cases of open fracture there were 13 amputations. The author states that injuries were caused by the explosion waves and shock rather than by the splinters of the mine. This factor was difficult to recognize without the aid of roentgenograms, which showed the extent of the damage and the fractures.

Albitskiy<sup>960</sup> discusses closed fractures of the foot due to explosion of land mines. He states that there is a typical appearance in these

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959. Stepanov, M. M.: Injuries of Lower Extremities Produced by Land Mine Explosion, *Khirurgiya*, 1945, no. 4, pp. 87-91.

960. Albitskiy, B. A.: Closed Fractures of Bones of Foot Due to Mine Explosions, *Khirurgiya*, 1945, no. 6, pp. 68-73.

fractures, as follows: shattering or demolition of the calcaneus, with wedging under the astragalus, which may itself be damaged; displacement upward of the rear fragment of the calcaneus by the pull of the achilles tendon and displacement forward of the front fragment by the short muscles of the foot. Luxations and subluxations in Chopart's joint and fracture of the metatarsal bones are explained by the action of the explosive wave on the front part of the foot, the midportion being strengthened by the leg. Fractures of the ankles also occur. The author does not recommend opening of the hematoma, since it leads to infection, but prefers prompt reduction and fixation in plaster casts. The author presents 8 illustrative cases, including instances of fracture of the calcaneus (with and without displacement), the astragalus, the cuboid bone, the metatarsal bones and the lower end of the tibia.

Bershon,<sup>961</sup> in discussing fractures of the feet and toes, points out that failure to follow generally accepted principles of the treatment of fractures may result in healing in malposition and disturbance of the function of nerves, blood vessels and tendons. He describes, in turn, fractures of the os calcis, the astragalus, the scaphoid, the cuneiform bones, the metatarsal bones, the toes and the sesamoid bones, and march fractures. He stresses recognition of accessory bones in the roentgenogram and states that 20 to 25 per cent of the feet of which roentgenograms were made in one series showed accessory bones. He also stresses proper reduction.

Borsotti<sup>962</sup> states that he treated 18 persons with 25 fractures of the calcaneus, who were in a bus under which a land mine exploded. He analyzes the fractures anatomically, discusses the various methods of therapy, reviews briefly the reports in the literature on the treatment and gives a brief case history of each of the 18 patients. He concludes that trauma from below produced characteristic fractures, as follows: Mild trauma produced fracture of the medial tuberosity; more serious trauma produced comminuted fracture of the posterior tuberosity and of the body of the calcaneus, with sinking of the head and subluxation of the astragalus and scaphoid between the anterior part of the calcaneus and the cuboid bone. Immobilization in a plaster cast was used in some cases and traction and casts in others, while amputation was done in the most serious cases.

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961. Bershon, A. L.: Fractures of Feet and Toes, *Bull. U. S. Army M. Dept.* 5:551-588 (May) 1946.

962. Borsotti, P. C.: The Treatment of Fractures of the Calcaneum Due to Trauma Acting from Below, *Minerva med.* 1:272-278 (April 14) 1946.

Cherry<sup>963</sup> reports 16 cases, reported between 1933 and 1940, of fractures of the os calcis in which treatment was by the Boehler method. Two patients could not be traced, 1 had died of tuberculosis four years after the fracture, 1 had multiple injuries and 3 had had type 1 injuries, according to the Watson Jones classification; the author reviews 7 cases of type 2 and 3 injuries (Watson Jones classification) in which the patients were seen four to nine years after the accident. He concludes that the end-result in nearly all cases was the same as before treatment, and that nothing is gained by the rather elaborate Boehler technic. He lists the disadvantages of this method: sepsis introduced through the pin tracts, osteoporosis, possibly due to heavy traction or to trauma by the redresseur, and wasting of the muscles of the calf and thigh.

[ED. NOTE.—The reviewer is inclined to agree with the author's statement that little is gained by accurate reduction in some cases; however, he cannot agree that the method of reduction is responsible for osteoporosis or wasting of muscles.]

Pridie<sup>964</sup> presents a new method for treatment of severe fractures of the os calcis by subperiosteal excision of the entire os calcis. He states that he used this method in 15 cases in three years and that excellent results were obtained in all except those of 2 older men with arteriosclerosis and arthritis. The technic for excision is given, with a description of the method of reinsertion of the achilles tendon in the plantar fascia. In each case, a plaster cast, applied with the foot in plantar flexion, was used for one month, at which time active non-weight-bearing exercises were begun. Weight bearing was begun at six weeks.

[ED. NOTE.—The first example of excision of the os calcis ever seen by this reviewer was that in a middle-aged dentist, who had bilateral excision of the os calcis in early childhood because of osteomyelitis. Function had always been good, and the man wore ordinary shoes without any type of correction. Many men injured in the war lost most or all of the os calcis; results were surprisingly good in cases in which the site was well covered with skin and soft tissue.]

Bado and Cagnoli<sup>965</sup> and Rapaccini<sup>966</sup> report on "duck bill" fractures of the calcaneus. The former authors noted 2 fractures of this

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963. Cherry, J. C.: Fractures of Os Calcis, *Irish J. M. Sc.* pp. 122-125 (April) 1946.

964. Pridie, K. H.: New Method of Treatment for Severe Fractures of Os Calcis: Preliminary Report, *Surg., Gynec. & Obst.* **82**:671-675 (June) 1946.

965. Bado, J. L., and Cagnoli, H.: "Duck Bill" Fracture of the Calcaneus: Pathogenesis and Therapy, *Bol. Soc. cir. d. Uruguay* **16**:243-261, 1945.

966. Rapaccini, M.: Contributions to the Study of Fractures of Posterior Superior Angle of the Tuberosity of the Calcaneum with Special Regard to Mechanism of Production, *Arch. ortop.* **56**:60-76 (July) 1940.

type in 270 cases of fracture of the calcaneus; the latter reports an incidence, for fractures of this type, of 2.64 per cent of all fractures of the calcaneus. Bado and Cagnoli state the belief that only those fractures involving the area of insertion of the achilles tendon can be of the avulsion type, whereas those above this area are caused by a flattening force. In treatment, closed manipulation is satisfactory for those fractures presenting only separation of the posterior ends of the fragments, but unsatisfactory when the fragment has been wedged. The latter type requires open reduction, with severing of the bony wedge by a chisel, after which the fragment is restored to its proper position. Severing of the achilles tendon will not restore a wedged fragment. Rapaccini considers it possible for this type of fracture to occur only in a congenitally predisposed calcaneus, with an unusually high insertion of the achilles tendon.

Negri<sup>967</sup> presents 2 cases of "duckbill" fractures of the calcaneus in patients with tabes dorsalis. In both cases, the fracture occurred as a result of a misstep; the author explains the mechanics of the fracture as the excessive pull on the achilles tendon by sudden and forceful contraction of the sural muscle, in an effort to prevent a fall.

Morrissey<sup>968</sup> reviews the current methods of treatment of fracture of the metatarsal bones and presents 61 cases in which treatment was with a simple molded leather arch, held to the foot by means of adhesive strapping. The method is discussed in detail. All the fractures in this series were due to direct trauma and all patients were men, whose ages ranged from 30 to 61, and who were engaged in various occupations. In 42 cases, there was fracture of only one metatarsal bone, in 11 cases, of 2, and in 8 cases, of 3 or more. Active weight bearing was begun immediately in more than one-half the cases and within a short time in the others. All patients returned to work of some kind within four days, and the majority returned to regular work in less than forty days; by the end of sixty days all had resumed their regular jobs.

[ED. NOTE.—This is a comprehensive report on treatment of fractures of the metatarsal bones; the original article should be consulted by those interested in this subject.]

*Fatigue, Strain and March Fractures.*—Bernstein and others,<sup>969</sup> who previously reported 307 cases, now add 692 more, among which are

967. Negri, E.: Fractures of Calcaneum, Avulsion Fracture May Be Symptom of Tabes Dorsalis: Two Cases, *Anteono parmense* **16**:294-296, 1945.

968. Morrissey, E. J.: Metatarsal Fractures, *J. Bone & Joint Surg.* **28**:594-602 (July) 1946.

969. Bernstein, A.; Childers, M. A.; Archer, M. C.; Fox, K. W., and Stone, J. R.: March Fractures of Foot: Care and Management of 692 Patients, *Am. J. Surg.* **71**:355-362 (March) 1946.

724 of march fractures of metatarsal bones. There was no evidence that a relatively shortened first metatarsal played any part in the occurrence of march fractures; the highest incidence occurred during the fifth and sixth week of training at an infantry replacement training center, a time when training was stepped up. Treatment consisted of the insertion of a steel bar longitudinally in the slip sole of the shoe. Only 58 patients did not respond to this treatment; 13 of these were hospitalized, and 45 were excused from training until the fracture healed. All 58 eventually finished training and were sent overseas. The author observed 426 fractures in the right foot and 298 in the left. The roentgenologic diagnosis is fully discussed.

Leveton<sup>970</sup> reports 12 march fractures of the pelvis and the lower long bones, excluding the metatarsals. Six were fractures of the tibia, 1 of the fibula, 2 of the femur (1 of the shaft and 1 of the neck) and 3 of the pelvis. The etiologic factors were obscure, but the author states the belief that the fractures were due to muscular fatigue or muscular imbalance. The ideal treatment was bed rest and the prohibition of early weight bearing. Delayed union was not encountered. The roentgenographic appearance was that of an "ice crack" fracture or of callus formation.

Levitin<sup>971</sup> reports 64 cases of march fracture of the articular surface of the tibial plateau. All the fractures were associated with pain. Forty-six cases were of fracture of the internal condyle and 18 were of the external condyle, a ratio of 2.6 to 1. The right knee was involved slightly oftener than the left. This fracture differs from other march fractures in that no bony callus forms to obliterate the fracture line during an observation period of six months. These injuries occur in civilian life but are so trivial that they are not usually examined roentgenologically until after osteoarthritic changes have taken place.

McPhee and Franklin<sup>972</sup> present 6 cases of march fracture of the fibula and 1 of the foot in athletes at Princeton University.

Nordentoft<sup>973</sup> presents 4 cases of march fracture, 1 each in the pubic ramus, the spinous process of the last cervical vertebra (clay shoveler's disease), the metatarsal bone and the femur.

Childress<sup>974</sup> presents a case of march fracture of the second metatarsal in a boy of 7. To this interesting case report the author appends

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970. Leveton, A. L.: March (Fatigue) Fractures of Long Bones of Lower Extremity and Pelvis, *Am. J. Surg.* **71**:222-232 (Feb.) 1946.

971. Levitin, J.: March Fractures of Articular Surface of Tibia and Its Relation to Osteoarthropathy, *Radiology* **46**:273-275 (March) 1946.

972. MCPhee, H. R., and Franklin, C. M.: "March Fracture" of Fibula in Athletes, *J. A. M. A.* **131**:574-576 (June 15) 1946.

973. Nordentoft, J. M.: March Fracture; Fatigue Fracture; Pseudofracture: Four Cases, *Ugesk. f. læger* **107**:391-394 (May 24) 1945.

974. Childress, H. M.: March Foot in a Seven Year Old Child, *J. Bone & Joint Surg.* **28**:877 (Oct.) 1946.



the following warning: "Had this patient been examined during the acute stage, a diagnosis might have been made of osteomyelitis or even of osteogenic sarcoma. March fracture always should be considered in osteoblastic lesions of the metatarsal bones, even in young children."

#### INJURY TO NERVES

Spurling<sup>975</sup> comments on the failure to treat injuries to nerves in patients with combined lesions of the nerve and bone during the North African and early European campaigns in the last war, with resultant useless members that could not be repaired in at least 20 per cent of cases. A program to provide early nerve suture was begun in December 1944; it entailed removal of patients to a neurosurgical hospital, early delayed closure of the primary wound and elective operation three weeks after healing of soft tissues. At the time of nerve suture, bone repair was done by the orthopedic member of the surgical team. About 10 per cent of patients required shortening or internal fixation of bones; 60 per cent required end to end suture of the damaged nerves and the remainder were treated by simple external and internal neurolysis. Twelve per cent of a total of 300 patients showed spontaneous recovery of the nerves during the waiting period. Final results are not given because of too short a follow up; prospects were excellent for recovery of the radial and sciatic nerves but less satisfactory for the recovery of the brachial plexus and the median and ulnar nerves.

#### COMPOUND FRACTURES

Brav and Fetts<sup>976</sup> studied 82 cases of gunshot fractures of the femoral shaft in a hospital in North Burma. Eighty-five per cent of patients were Chinese. There was a 4.9 per cent mortality; bone union occurred in 96 per cent of the cases.; good functional results were obtained in 67 per cent of the followed cases, fair results in 24 per cent and poor results in 9 per cent. Skeletal traction in balanced suspension is the method approved by the authors for fixed installations; the use of a plaster spica is their choice for temporary immobilization. Traction should be continued until there is roentgenologic evidence of bony union; the average time required was twelve weeks. Motion of the knee joint should be encouraged after eight weeks.

Obletz<sup>977</sup> recommends "90-90-90 traction" as an aid to operative management, as it permits easy approach to all soft tissue wounds

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975. Spurling, R. G.: Early Treatment of Combined Bone and Nerve Lesions, *Physiotherapy Rev.* **25**:287-288 (Nov.-Dec.) 1945.

976. Brav, E. A., and Fetts, W. T., Jr.: Gunshot Fractures of Femoral Shaft, *Surg., Gynec. & Obst.* **82**:91-100 (Jan.) 1946.

977. Obletz, B. E.: Vertical Traction in Early Management of Certain Compound Fractures of Femur, *J. Bone & Joint Surg.* **28**:113-116 (Jan.) 1946.

as well as to the fracture focus in the treatment of compound fractures of the femur. The hip, knee and ankle are all in 90 degree flexion; the patient is in dorsal recumbency, with Kirschner wires inserted through the condyles of the femur or the tibial tubercle, for vertical traction to an overhead bar; for operative procedures, the foot is held by a sock attached to the overhead bar. The same position can be maintained in bed with a 10 pound (4.5 Kg.) weight horizontally on a standard Pearson knee attachment, with foot rest. The author recommends the use of this position for only three to four weeks, after which conventional splints should be used.

Soto-Hall and Horwitz<sup>978</sup> review 163 cases of fractures of the femur, in which 117 were compound and 46 simple fractures; 41 were treated by internal fixation and 122 by suspension traction. The authors conclude that early and adequate débridement is the most vital factor for successful treatment in compound fracture, that chemotherapy may control infection but is useless in the presence of necrotic tissue and that delayed wound suture and conservatism in the removal of large bone fragments are desirable. Extremely gratifying results were obtained with traction in balanced suspension. Early internal fixation in the presence of an open wound was hazardous. Early use of active exercise with carefully supervised resistive exercises aided knee function.

#### OPERATIVE FIXATION OF FRACTURES

*Medullary Nailing.*—Much interest has been shown in this treatment in the past few years. D'Aubigne and Lance<sup>979</sup> used intramedullary nailing in 17 cases of diaphysial fracture of the femur. Treatment in all cases was by opening of the focus of the fracture. The authors state that they prefer to insert the nail from the fracture into the proximal fragment, reducing the fracture and then running the nail into the distal fragment. They recommend a nail used by Ivar Palmer of Stockholm. They state that they operated thus in 17 cases of ancient fractures of the femur (5 fractures had previously been plated). Fractures in 3 cases were recent and loss of bone had taken place in 2. Of the patients in the remaining 12 cases, 8 of which had war wounds, 11 had normal consolidation in three months; 3 of these had slightly hypertrophic callus. Knee motion was almost complete in 5, and greatly limited in 7.

Boppe and Adam<sup>980</sup> report the use of Küntscher's intramedullary nailing in the treatment of 20 fractures of the femoral diaphysis, 14 of

978. Soto-Hall, R., and Horwitz, T.: Treatment of Compound Fractures of Femur, J. A. M. A. **130**:128-134 (Jan. 19) 1946.

979. d'Aubigne, R. M., and Lance, P.: Results of Medullary Nailing in Fractures of Femur, Mém. Acad. de chir. **72**:370-372 (June 19-26) 1946.

980. Boppe, and Adam: Küntscher Nailing in Fractures of Femur, Mém. Acad. de chir. **72**:372-374 (June 19-26) 1946.

which were recent and 5 ancient. Pseudarthrosis of the femur occurred in 1 case six and a half months after nailing. Of the 14 cases of recent fracture, 7 were in adults and 7 in children. In 7 cases the nailing was percutaneous, and in 7 the fracture site was opened. The authors were striving to improve their technic so that percutaneous nailing could be used in all cases. The cases were followed for two to eighteen months after operation. In most cases the nails were still in situ, and healing in all was without incident.

Huet<sup>981</sup> makes it clear that he does not favor the use of the Küntscher nail. Basing his argument on the experiences of his pupils who were forcibly detained in German hospitals for some time and who saw the Küntscher method used, he counters all claims for intramedullary nailing. He concludes that the Küntscher method is not an improvement over osteosynthesis with plate and screws or over the older methods.

Leveuf and Laurence<sup>982</sup> report 13 cases of intramedullary nailing of diaphysial fractures of the femur in children from 2 to 13. In all cases, it was necessary to open the fracture site. The authors used the angle nail made by Drapier and the Rocher round nail; nails were removed in all cases in three to four months. Late results were excellent. The authors state the opinion that indications for intramedullary nailing are irreducible fractures of the middle or upper third of the femur, and vicious malunion and pseudarthrosis.

Uffreduzzi<sup>983</sup> reports his experiences and states that Küntscher's method has the decided advantage of interfering less with consolidation and with callus formation than any type of appliance used on the outside of the bone. The author prefers a long, slender rod, which he believes causes very little damage to the contents of the medullary canal. It is possible to insert the prosthesis at a distance from the focus of the fracture. Favorable results are reported, and the author states that this method can be applied to gunshot wounds that are not too badly contaminated or infected.

Jeanneney, Magendie and Tingaud<sup>984</sup> report a very interesting series of cases of fracture in which treatment was by the Küntscher method

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981. Huet, P.: Küntscher Nailing in Fractures of Diaphysis of Femur, *Mém. Acad. de chir.* **72**:400-403 (July 3-10) 1946.

982. Leveuf, J., and Laurence, G.: Results in Intermedullar Nailing by the Method of Küntscher in Fractures of the Femoral Diaphysis, *Mém. Acad. de chir.* **72**:368-369 (June 19-26) 1946.

983. Uffreduzzi, O.: Fixation by Intramedullary Nailing, *Gior. d. r. Accad. di med. di Torino (parte seconda)* **105**:89-95 (July-Sept.) 1942.

984. Jeanneney; Magendie, and Tingaud: Late Results of Medullary Nailing of Diaphyseal Fractures According to Küntscher Method, *Bordeaux chir.* **3-4**:63-74 (July-Oct.) 1943.

and that of Rocher, using a solid steel rod. The authors state that there was excellent tolerance of the rod in 3 cases. Signs of decalcification in 1 case were probably due to the mobility of the rod, and in 2 cases in which ordinary steel was used there was oxidation. The authors state the opinion that intramedullary nailing, whether done because of destruction of the medulla or for some other reason, appears to cause a retardation in the callus formation. For this reason the fixation should be continued at least a month longer than the usual period. The authors recommend the method as ideal in treatment of fractures of the bones of the forearm and of the femoral shaft.

Rocher <sup>985</sup> reports on 22 cases, all of difficult fractures or of failures in treatment by other methods. He states that no patient of his has ever had a painful sequela following nailing or withdrawal of the nail; neither infection nor fat emboli have been observed. He reports 2 cases in which there was a loss of bone substance; osseous tissue grew out along the nail and filled the loss completely. He is of the opinion that, with sufficient experience, this method is the simplest and best for treating the average fracture.

In view of the controversy over the intramedullary pegging of bone, Chigot <sup>986</sup> conducted a series of experiments on rabbits and dogs, using autoplasmic, homoplasmic and heteroplasmic pegs. In certain animals he observed fusiform periosteous hypertrophy, noted by others in human patients; the growth was fleeting and inconstant. Resorption of the peg was remarkably clear in certain instances, but irregular. Histologic study showed a fibrous reaction of the medulla, but complete restoration and no cicatrix. The periosteum, not the medulla, is the bone-making organ, and an intramedullary foreign body is much less harmful to the bone than a periosteal plate. The author discusses changes in the materials used for intramedullary pegs since his previous report in 1937; he now states a preference for bone and uses dealbuminated pegs. He states that he finds the use of the Küntscher nail difficult on the femur. In the treatment of fractures of both bones of the forearm, he states that he prefers to use a Kirschner wire in the ulna and a dealbuminated bone peg in the radius. The wire is inserted first; it is pliable enough to permit angulation of the radius for insertion of the bone peg. The extremity is treated in a plaster cast.

[ED. NOTE (W. G. S.).—Here we are back to the intramedullary bone graft.]

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985. Rocher, C.: Medullary Nailing of Long Bones: Reflection on Twenty-Two Cases, *Bordeaux chir.* **1-2**:80-81 (Jan.-April) 1944.

986. Chigot, P. L.: Intramedullary Diaphysial Osteosynthesis by Means of Pegging, *Presse méd.* **54**:89-91 (Feb.) 1946.

Soeur,<sup>987</sup> in an excellent article, discusses the historical background of the intramedullary fixation and calls attention to the fact that Lambotte has been using the method since 1907 without recognition of the fact by American surgeons. The author cites the objections for and against the method and takes up individually the treatment of fractures of the various long bones, discussing the method to be utilized in managing each of these fractures. He recommends intramedullary fixation because it fulfills the three principles of treatment, namely, reduction, which is usually excellent; fixation, which is strong and firm, and mobilization, which is rapid. In 55 cases of fracture reported, there were 23 of the shaft of the femur, 10 of the leg, 9 of the humerus and 13 of the forearm; the results were excellent. The author feels that the method is particularly applicable to fractures of the femur and forearm and that it solves problems not met satisfactorily by other methods. He does not, however, advise its use in the treatment of compound fractures.

Floding<sup>988</sup> reports on 15 cases in which treatment was by intramedullary nailing according to the method of Küntscher. The study consists of a review of Küntscher's method, its advantages and the indications for its use as given by Küntscher himself, together with a description of the instruments necessary and a number of case reports. In this discussion, there is comparatively little in the way of critical evaluation of the procedure.

Magnant<sup>989</sup> reports on treatment of 13 fractures by the Küntscher method and states that it is better to use a Kirschner wire than a heavier pin in the treatment of fractures of the clavicle. The author states that he prefers the cylindric rods of Rocher. Fractures of the femur may be nailed without opening the fracture. Of 6 cases in which the leg was involved, a small opening at the site of fracture was necessary in only 3. Magnant stresses the noninterference with callus formation, the much earlier restoration of function in the extremity and the excellent tolerance of the nail in the tissue in his cases in which treatment was by this method.

Leger and Crepin,<sup>990</sup> on the other hand, report 11 cases in which they used the Küntscher nail. In only 1 case in this series was the fracture nailed without opening the site of the fracture. The authors

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987. Soeur, R.: Intramedullary Pinning of Diaphysial Fractures, *J. Bone & Joint Surg.* **28**:309-331 (April) 1946.

988. Floding, A.: Fractures of Long Bones Treated with Medullary Nailing According to Küntscher, *Nord. med.* **30**:1179-1183 (May 31) 1946.

989. Magnant: Küntscher Method of Nailing Long Bones: Late Results, *Mém. Acad. de chir.* **72**:378-379 (June 19-26) 1946.

990. Leger, L., and Crepin, G.: Küntscher Nailing, *Mém. Acad. de chir.* **72**:375-376 (June 19-26) 1946.

defend this procedure on the ground that more damage would have been done in the treatment of fractures of great displacement by manipulation and closed reduction; in 1 case the radial nerve was caught between the fragments. They state the belief that the best indication for this method is pseudarthrosis and that spiroid fractures of the leg are a contraindication. The nailing of a fracture of the humerus is the easiest use of Küntscher's method. The nailing of the femur is facilitated by the use of the scissors position recommended by Christian Rocher.

*Guides and Devices for Internal Fixation.*—Stone<sup>991</sup> presents a guide for the nailing of fractures of the femoral neck, consisting of a steel bar attached to and extending upward from a nail driver at 90 degrees and a clamp which holds the guide rod parallel to the nail driver. The author claims that its advantages are that the direction of the nail is visible to the operator, that no part of the guide enters the operative wound, that operative time can be shortened and that the use of the guide eliminates repeated roentgenographic check-ups.

Hopkins<sup>992</sup> presents a detailed description of a block guide which is attached to the external surface of the femur after reduction to serve in directing the proper placement of a nail in the femoral head and neck.

*Fractures Treated by Continuous Wire Traction.*—Kirby and Fitts<sup>993</sup> report their experiences in 342 cases in which treatment was given at a general hospital in India. In this series, 194 patients were treated with Kirschner wires, 95 with Steinmann pins and 52 with Roger Anderson pins with fixed or balanced traction. Among those patients treated with Kirschner wires, 4 wires grew loose from the bone and 1 broke in fourteen weeks. The bow slipped and the wire pulled out in eight weeks in an additional case. With the Steinmann pin the results apparently were quite satisfactory, although an abscess developed in 1 case and there was transient peroneal paralysis in 2 cases. In the group treated with the Roger Anderson pin 3 pins became loose. In none of the cases did the complications have any significant effect on the course of the treatment or the final result. The authors consider that the use of transfixion pins and wires for skeletal traction is a safe and reliable procedure.

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991. Stone, M. M.: Visible Guide for Nailing Intracapsular Femoral Neck Fractures, *Am. J. Surg.* **71**:100-102 (Jan.) 1946.

992. Hopkins, H. H.: Intertrochanteric Fractures and Fractures of Neck of Femur: A Guide and Method of Procedure for Accurate Placement of Nail, *J. Bone & Joint Surg.* **28**:244-249 (April) 1946.

993. Kirby, C. K., and Fitts, W. T., Jr.: Incidence of Complications in Use of Transfixion Pins and Wires for Skeletal Traction, *Ann. Surg.* **123**:27-31 (Jan.) 1946.

Schildt,<sup>994</sup> in a comprehensive article covering his experience in the treatment of 540 fractures by wire traction, states that complications in the form of nerve injuries, cutting of the wires, infection or necrosis were encountered in only 10 per cent of the cases. Prognosis of the nerve injuries is likely to be very favorable. Cutting of the wires through tissue was noted in 18 cases; the disadvantage of this is slight unless the cutting is in the lower end of the femur, when it may lead to menacing and serious complications because of damage to the knee joint. Infections without cutting of the wire were observed in 30 cases of 504 (6 per cent), but the infection was slight to moderate and had no disastrous effect on the course of the treatment. The author states that wire traction in the calcaneus is practically free of risk. Complications in cases in which wire traction is used in the tuberosity of the tibia are fairly numerous, but not serious. The author calls attention to the necessity of preventing lateral slipping in the wire and states that the points of exit and entrance must be protected with a snug bandage to assist in the prevention of infection.

Dwyer and Murry<sup>995</sup> review the treatment of fractures at the Northern Permanente Hospital, Vancouver, Wash., from September 1942 to December 1944. In this period, 1,418 fractures were seen. Of this number, 131, or 9.2 per cent, were treated by skeletal traction and 121, or 8.5 per cent, by dual pin fixation. The Roger Anderson equipment was found most desirable for use with the dual pin method. Kirschner wire and the Kirschner-type tautner were used for skeletal traction. Continuous skeletal traction was used mainly for fractures of the hands and feet. Dual pin fixation was used chiefly in fractures of the tibia, fibula, femur, mandible, os calcis and humerus. In this series, osteomyelitis developed in 2 cases of hematogenous origin and 1 of external origin. There were 4 instances of delayed union, 4 of malunion and 3 of nonunion in the entire series, or unsatisfactory results in 4.4 per cent of the cases.

Scott<sup>996</sup> also makes a plea for greater use of the external fixation treatment of fractures, stating that it is much easier and less hazardous than some of the older and more generally accepted methods of treatment. The author states that the treatment of compound fractures is facilitated by this method. He cites as an advantage the reduction in the number of stiff joints after immobilization.

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994. Schildt, E.: *Complication of Wire Traction Treatment*, Nord. med. (Hygiea) **29**:301-307 (Feb. 8) 1946.

995. Dwyer, F. J., and Murry, D. H.: *Therapy by Skeletal Traction or Dual Pin Fixation: Two Hundred and Fifty-Two Cases*, Northwest Med. **45**:173-177 (March) 1946.

996. Scott, I. H.: *External Skeletal Fixation*, Am. J. Surg. **72**:723-733 (Nov.) 1946.

Roberts<sup>997</sup> reports the treatment of mandibular fractures by means of the Roger Anderson external splint. The author says that use of this apparatus provides an excellent form of treatment for certain types of jaw injuries. He states the belief that the method should be used only by responsible surgeons working under proper conditions, lest it be discredited; it is not the method of choice when simpler methods will give equally satisfactory results. The author's opinion is shared by Burke, Murphy and McNichols,<sup>998</sup> who state that Roger Anderson apparatus is particularly adaptable to the treatment of certain types of mandibular fractures which cannot be treated satisfactorily by other methods.

#### GENERAL FACTORS IN TREATMENT OF FRACTURES

Dickson,<sup>999</sup> in a practical article, calls attention to the use of physical therapy in the treatment of fractures. The place of occupational therapy is stressed.

Engh<sup>1000</sup> reports on a series of roentgenograms of fractures in and about the joints, in the treatment of which he used vitallium screws for fixation. The author does not recommend this method as one of choice but states that it is possible to fix fractures in these areas by this means and that the end results can be excellent.

Anopol<sup>1001</sup> stresses that treatment of fractures should be simple, direct and practical and emphasizes the value of fundamental principles of therapy as applied to each individual case. He reminds the reader that good reduction is not enough when the soft tissues are injured, that methods used experimentally on animals cannot be transferred directly to the treatment of human beings and that the functional position of each joint must be considered when there is a possibility of ankylosis. He deplores the present trend of the "gadget treatment" of fractures.

Verbrugge,<sup>1002</sup> in a comprehensive article concerning factors influencing callus formation in open fixation of fractures, emphasizes the

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997. Roberts, W. R.: Control of Mandibular Fragments by External Fixation, *Brit. Dent. J.* **80**:257-269 (April 18); 291 (May 3) 1946.

998. Burke, H. D.; Murphy, D. L., and McNichols, W. A.: Skeletal Fixation of Mandibular Fractures: Five Cases with Nine Fractures, *Arch. Surg.* **51**:279-282 (Nov.-Dec.) 1945.

999. Dickson, F. D.: Physical Therapy in the Treatment of Fractures, *Rev. radiol. y fisioterap.* **13**:17-21 and 35 (Jan.-Feb.) 1946.

1000. Engh, O. A.: Screw Fixation of Fractures, *J. Internat. Coll. Surgeons* **9**:144-151 (Jan.-Feb.) 1946.

1001. Anopol, G.: Therapy in Fractures, *Bull. internat. serv. san.* **19**:91-93 (March) 1946.

1002. Verbrugge, J.: Factors Influencing Callus Formation in Open Fixation, *J. Bone & Joint Surg.* **28**:535-543 (July) 1946.



importance of performing open fixation as soon as possible after injury. When operation is not carried out until fifteen days after the fracture the optimum time is lost for early callus formation and for early union of the fracture. The author also discusses the nature of the internal fixation used and its physiologic application to the fracture. He states that other factors influencing callus formation are early function, sympathectomy, ganglionectomy, massage, the administration of calcium and short wave diathermy.

Darrach,<sup>1003</sup> in a well written, didactic article, emphasizes nothing new but calls attention to the old principles which underlie all treatment of fractures, namely, (1) reduction of secondary trauma to a minimum, (2) sufficient restoration of normal form to meet the requirements of the specific patient, (3) rest for the fractured part during the healing process, (4) maintenance and restoration of the function of the soft parts and (5) maintenance of the morale of the patient. The author also emphasizes the fact that the patient must be treated as an individual human being and not simply as a fractured bone of one kind or another.

Sweetapple<sup>1004</sup> discusses the clinical features, etiology and treatment of Sudeck's atrophy but fails to add any definite information not already known. [ED. NOTE (W. G. S.).—This is a general article and reviews the subject well.]

Hojensgaard<sup>1005</sup> calls attention to the frequency of secondary dislocations in cases of fractures of the distal end of the radius. In a series of 217 cases of such fractures, redislocation was noted in 52 cases, or 24 per cent of the total. The author suggests that the average rate of incidence may be still higher. These fractures are classified in seven groups, according to type. Dislocation occurs most frequently in cases in which a distal fragment shows volar dislocation and in comminuted Colles' fracture. A statistical tabulation shows that redislocation is most likely to occur in women past 60. The author recommends the following procedure as a means of preventing redislocation: (1) roentgenographic control; (2) avoidance of a loose bandage, due to swelling at the time of application (replacement with a snug bandage should be done as soon as possible); (3) application of a well padded circular cast and (4) fixation for an adequate period (four to five weeks as a minimum.)

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1003. Darrach, W.: Presidential Address, *Ann. Surg.* **124**:607-616 (Oct.) 1946.

1004. Sweetapple, H. A.: Sudeck Atrophy, *M. J. Australia* **2**:581-584 (Oct. 26) 1946.

1005. Hojensgaard, I. S.: Frequency of Secondary Dislocation in Fractures, *Nord. med. (Hospitalstid.)* **28**:2135-2139 (Oct. 19) 1945.

Teece,<sup>1006</sup> in discussing the procedures and attitudes in handling orthopedic disorders in industrial patients, gives no specific formula to solve this problem. He states that the attitude of the medicolegal patient differs according to race and occupation. Aside from this factor, there are two types of patients who are not often encountered in ordinary practice, namely, the fulsome, cooperative patient and the suspicious, exaggerating patient. The former talks volubly of his injury, and the latter practically refuses to discuss it, apparently believing that the examining physician is in league with the insurance company and striving to deprive him of his rights and his compensation. As for actual treatment of the orthopedic conditions seen in industrial practice, there are no notable differences as compared with treatment in the rest of the community. The author states the belief, however, that the chief emphasis is on function rather than on appearance. Injuries to fingers are very common in industrial work, and the question of early amputation frequently arises. The object of primary treatment should always be to save as much as possible of every digit. The author believes that malingering is rather rare but that some patients, in the course of long treatment, become afraid to use the injured part and assume that recovery may not be complete. Other patients acquire the habit of idleness during a long period of inactivity with compensation and lose the will and desire to return to work.

#### COMPOUND FRACTURES

Rounds<sup>1007</sup> discusses treatment in 551 cases of war injuries recorded in a general hospital in England, in which various modifications of the Orr-Trueta treatment were carried out. He states that successful secondary closures can be performed after the Orr treatment has been meticulously carried out at the front station. He suggests that the best time for secondary closure is on the fourth or fifth day after injury; the average time of closure in this series was on the twelfth day. Healing took place in 90 per cent of the cases; it was apparently unaffected by the use of penicillin, although the drug was used in the worst cases.

Eaton<sup>1008</sup> reports on the routine treatment of compound fractures of the long bones in the campaigns of World War II. He stresses the importance of first aid and shock therapy even before the patient is moved to the clearing company from the battalion aid station. The first operation performed at the forward station was careful débridement

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1006. Teece, L. G.: *Special Characteristics and Requirements of Orthopaedic Surgery*, M. J. Australia **2**:580-581 (Oct. 26) 1946.

1007. Rounds, R. C.: *Delayed Suture of Wounds Associated with Fractures*, Rocky Mountain M. J. **43**:216-219 (March) 1946.

1008. Eaton, G. O.: *Overseas Treatment of Compound Fractures of Long Bones*, J. Bone & Joint Surg. **28**:434-439 (July) 1946.

of the wound, consisting of thorough exposure and exploration of all tracts and excision of all devitalized tissues, decompression and aeration of the wound, generous incision and relaxation of the fascial layers (with great care to preserve as much skin as possible), counterincisions for dependent drainage and complete removal of all fragments of bone completely denuded and unattached. The author recommends not suturing the injured tendon or nerves but marking them for later suturing. After débridement the wound is left wide open, with no attempt at partial closure. Eaton stresses particularly that the wound must not be closed in the early stage at the forward station.

Bintcliffe,<sup>1009</sup> who was stationed at a base hospital rather than at a forward station, describes the receipt of patients. He emphasizes the importance of using penicillin. He is particularly concerned with the subject of delayed primary suture or so-called secondary suture of the wounds which have undergone careful and prompt débridement and been left open. Further limited débridement was carried out if necessary but often was totally unnecessary. The author describes 30 cases in which suturing was done one to eighteen days after injury. In 17 cases the wound was completely healed in fourteen days; in 9 cases there was some delay in healing, and in only 4 cases was there failure of the wound to heal, accompanied with breaking down, necrosis or sequestrum formation. Bintcliffe, too, stresses the importance of the surgical operation performed at the front station, after which the wound is left open, no attempt being made to close it.

Hampton<sup>1010</sup> discusses 332 cases of fractures in which treatment was by various types of delayed internal fixation, which are described. He suggests that all these forms of internal fixation should be carried out only after primary or secondary closure and healing of the wound. The author provides a detailed discussion of 20 cases, with illustrations.

Novachenko,<sup>1011</sup> in discussing fractures treated at the finish of the war, states the belief that it is possible to note certain peculiarities or characteristics of gunshot injuries as opposed to those caused by other etiologic agents. He describes the classic form of this type of the fracture as a butterfly wing; the fracture is shattered in character, leaving sequestrums of bone, which may be a complicating factor. This type is characterized also by pronounced displacement of the fracture and by the scattering of fragments of bone throughout the soft tissue. Another peculiarity is that of bone regeneration. The author notes that

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1009. Bintcliffe, E. W.: Delayed Closure of Compound Fracture Wounds, *Post-Grad. M. J.* **21**:338-348 (Dec.) 1945.

1010. Hampton, O. P.: Delayed Internal Fixation of Compound Battle Fractures in the Mediterranean, *Ann. Surg.* **123**:1 (Jan.) 1946.

1011. Novachenko, N. P.: Characteristics of Gunshot Fractures, *Vrach. delo* **24**:47-52 (Dec. 1) 1944.

gunshot fractures apparently healed as fast as closed fractures, in spite of the general belief to the contrary. There was, however, certain characteristic lingering of different stages of callus formation, the completion of which seemed to take somewhat longer than usual. The author recommends treatment as early as possible, directed primarily toward prevention of infection and secondarily toward repair of the fracture; this type of fracture can be treated by reduction, use of a plaster cast, skeletal traction or various other methods.

Faltin <sup>1012</sup> directs his attention particularly to two types of fractures. The first group is composed of those about the face; the author stresses the importance of proper first aid and early treatment at a field hospital, preliminary to definitive treatment at a special hospital for maxillary surgery. The sooner the treatment is begun, the better result will be obtained. The second group, in which the author has particular interest, is that composed of fractures of the hands and fingers. The author stresses the importance of special centers where definite treatment can be given to the hand by those especially skilled, since passive treatment has too often resulted in useless fingers.

Carney, Fitts and Kirby <sup>1013</sup> direct their attention to gunshot injuries of the joints as opposed to fractures of the long bones, noting that treatment of these injuries is usually difficult and that results are often disappointing. The authors studied 134 cases of gunshot wounds of the major joints in which there was a complicating fracture of the adjacent bone. No particulars are given because the follow-up was too short to be of any value in analyzing the permanent result. These authors, too, stress the importance of careful débridement and removal of all foreign bodies. Ordinarily the capsule should not be closed primarily but by secondary closure, in order to minimize infection. The authors state that fusion of the joint should be postponed, since improvement will often follow after many months, or even years.

Compere <sup>1014</sup> discusses the treatment of compound fractures in civil life with particular emphasis on the way they have been maltreated in many instances. He gives a detailed outline of the care of the compound wound, stressing the importance of the care given by the general practitioner who sees these wounds immediately after their occurrence; he recommends careful splinting before arrival at the hospital, careful débridement and lavage. He discusses the problem of primary or secondary closure of the wound, giving the indications and contraindications for each procedure.

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1012. Faltin, R.: Contribution to the Solution of Several Problems in Military Surgery, *Nord. med.* **17**:91-98 (Jan. 16) 1943.

1013. Carney, P. W.; Fitts, W. T., and Kirby, C. K.: Gunshot Wounds of the Major Joints, *J. Bone & Joint Surg.* **28**:607-615 (July) 1946.

1014. Compere, E. L.: Adequate Treatment of Compound Fractures, *Illinois M. J.* **88**:289-293 (Dec.) 1945.

[ED. NOTE (W. G. S.).—In considering all these articles together, certain major points of agreement are at once evident. The authors are unanimous in stating, at least with regard to war surgery, that grossly contaminated gunshot injuries should be treated by débridement of the wound, after which the wound should be left open and careful support supplied to the wound and the extremity; secondary or delayed closure should be done from one to two weeks subsequent to the original operation. Disagreement exists as to whether or not loose fragments of bone should be removed, the majority of writers stating the opinion that they should be. There is considerable unanimity in the opinion that tendons and nerves should be marked at the primary operation, but should not be sutured, and that internal fixation was inadvisable at the time of the secondary closure but should be done after healing. All the authors stressed repeatedly the importance of general systemic care of the patient.]

In concluding this subject, it is well to mention an article by Cleveland,<sup>1015</sup> in which he gives a comprehensive review of the treatment of the wounded, in general, in World War I and in World War II. The author describes the preparation at the orthopedic centers for care of the wounded with injuries of bones and joints, the fixed hospitals in the zone of communication, the treatment of severe multiple fractures and the healing of compound fractures, amputations and neurosurgical injuries and injuries to the hands. He makes the following observation:

Having served as a medical officer in both wars, it may be permissible to make a few comparisons. The 25 years which elapsed between the wars has seen progress in the training of the young surgeons and this was reflected in the fact that more and better trained surgeons were available to do better surgery. There never were enough to completely fill all the existing vacancies, but the situation was vastly improved over World War I. In the European Theater the general level of care of bone and joint casualties was vastly improved. Superior care was unquestionably rendered by many of the affiliated hospitals of World War I, but in other less favored units it left much to be desired. There was a more complete and general understanding of resuscitation in World War II. No blood or plasma was available or used in most of the Army hospitals in World War I. The great stocks of plasma and whole blood which were made available and were used so extensively saved many of the wounded who would otherwise have succumbed.

The evacuation of the wounded in World War II was more rapidly accomplished.

The overseas hospitals were very much better equipped for their work in this war. The low incidence of infection was probably due to better surgery in the forward areas. In this matter of lower infection, the role of sulfonamides and penicillin is not absolutely clear. These new drugs probably exerted a beneficial effect, but controlled experimental data is not available.

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1015. Cleveland, M.: Orthopedic Surgery in the European Theater of Operations, *Ann. Surg.* 124:188-200 (Aug.) 1946.

The European Theater was singularly fortunate in having a Chief Surgeon whose sole aim was to improve the standard of care of the sick and wounded American soldier. Nothing deterred him from this aim. The professional service division had a group of consultants who worked harmoniously as a team under inspiring leadership of the Chief Surgeon and the Chief Consultants in Surgery and Medicine.

#### FAT EMBOLISM

Warren<sup>1016</sup> presents a review of 100 consecutive fatal cases of fat embolism recorded in the files of the Army Institute of Pathology in four years (1941 to 1944); 82 per cent of these were due to fractures of the tibia or the femur. The author calls attention to the fact that embolism is due not to aggregation of circulating fat, but to quantities of fat set free from bodily deposits. Death was instantaneous in 9 of the cases; it occurred after symptoms of immediate origin in 17 cases and was delayed in 58. The occurrence of fat embolism is apparently uninfluenced by the nutritional state of the patient. The condition may be recognized by development of pulmonary or cerebral symptoms following fracture or extensive injuries of soft parts, or manipulation of a fracture. The renal fat embolism may be pronounced, but renal failure is not the cause of death. Many nonfatal cases of fat embolism are not recognized, and many fatal cases may be unrecognized unless a search is made for the cause of death.

Lindsay and Moon<sup>1017</sup> present 3 cases in which bone marrow embolisms were found in the arteries in the lungs of men who died after accidents in which they received multiple fractures. The embolisms were found in examinations of sections taken from the lungs at necropsy. The authors point out that although some 600 cases of fat embolism have been reported, the condition usually occurring after fracture of the long bones, only 1 case of associated bone marrow embolism to the lungs has been reported. This report is of interest, but no particular recommendation for prevention or treatment is included.

#### FRACTURES OF THE SPINE

Daniels<sup>1018</sup> discusses, in some detail, the management of fractures and dislocations of the spine in warfare, basing his article largely on his personal experience while in the Navy. He discusses many problems rather unique to the service, including evacuation of the injured person and his rapid transportation to a first aid station. In most instances patients were examined at first aid stations within fifteen minutes after injury. The author seems well satisfied with the method of handling

1016. Warren, S.: Fat Embolism, *Am. J. Path.* **22**:69-87 (Jan.) 1946.

1017. Lindsay, S., and Moon, H. D.: Bone Marrow Embolism Following Fracture, *J. Bone & Joint Surg.* **28**:377-380 (April) 1946.

1018. Daniels, J. T.: Fractures and Dislocations of the Spine in Warfare, *Am. J. Surg.* **72**:414-423 (Sept.) 1946.

this type of injury in the service and points out that it was greatly improved over that in World War I. A rather detailed description is given of the method of handling these patients, both on land and on sea, and of the causative factors in various types of war injuries. Laminectomy is recommended when there is evidence of any progression of cord dysfunction with pressure of a fragment, either of bone or of a foreign body, on the cord, or when there is an irreducible dislocation, particularly if it involves the area of the lower cervical and upper dorsal portions of the spine.

Guthkelch<sup>1019</sup> calls attention to the fact that the ordinary fracture and dislocation of the cervical portion of the spine must be reduced by both traction and extension. He describes a method of successful reduction by skeletal traction. Some points of technic are different from those ordinarily suggested: The traction apparatus is placed in the skull, forward of the external auditory canal, thus increasing the extension on the upper cervical part of the spine; countertraction is secured by the patient's sitting against a back rest at an angle of at least 60 degrees. After reduction, of course, the traction is rapidly released, and after about four weeks a plaster cast is used.

Denis<sup>1020</sup> describes the use of open reduction in the treatment of irreducible dislocation of the cervical portion of the spine, using the method (similar to that described by Davis) of open reduction by direct visualization, in which the articular surfaces are levered apart and the dislocated vertebra then fastened to the adjacent intact vertebra with wire. The author even advises this method in paraplegia and cervical quadriplegia.

Ingebrigtsen<sup>1021</sup> discusses the same problem at some length. His experience was rather unsatisfactory, since 3 of the 4 patients operated on died. He obtained a satisfactory result in the successful case: In spite of the fact that the patient had complete paraplegia in the initial stages, he made an almost complete recovery; this case has been followed for some thirteen years. The author concludes that fractures and dislocations of the spinal column, with neurologic symptoms, including a complete transverse lesion, should be treated by immediate open reduction. In cases in which the cord has been completely crushed the operation will be of no avail, but if complete crushing has not occurred the operation may be the means for rehabilitation of the patient.

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1019. Guthkelch, A. N.: Management of Recent Fracture-Dislocations of the Cervical Spine, *Brit. M. J.* **2**:880-881 (Dec. 22) 1945.

1020. Denis, R.: Treatment of Dislocations of the Cervical Spine by Traction, *Mém. Acad. de chir.* **72**:349-352 (June 19-26) 1946.

1021. Ingebrigtsen, R.: Dislocation and Fracture-Dislocation of the Spinal Column, *Acta chir. Scandinav.* **94**:455-469, 1946.

Boorstein<sup>1022</sup> discusses a series of compression fractures, basing his review on 160 cases. His is a comprehensive study, in which the degrees of compression fracture are described as mild, severe and central; cases are classified according to sex and occupation of the patient, area of the spine and nerves involved, treatment and results. Routine treatment in these cases was rest on a Bradford frame in a hyperextended position, followed by immobilization in a plaster jacket or two plaster shells and, finally, use of a spinal brace. Attention is called to the fact that full recovery may take from one to two years. The author is in agreement with Daniels<sup>986</sup> in stating that early operation should be performed when a dislocation is present or when a fragment of bone is pressing on the canal. However, in this series, 9 of 11 patients having laminectomy died.

In discussing the complications in the various types of fractures and fracture-dislocations with damage to the spinal cord, Christensen<sup>1023</sup> concludes that whenever possible an automatic bladder should be allowed to develop before the patient is catheterized. The author calls attention to the fact that this procedure has been recommended by many surgeons in the past, that there is no danger of rupture of the bladder and that the bladder empties well after use of this method for three or four days. On the other hand, repeated catheterization or the use of an indwelling catheter too frequently causes urinary infection.

Brage<sup>1024</sup> describes 1 case, in which he diagnosed an avulsion of the tubercle of the transverse apophysis of the first dorsal vertebra. Some confusion arose, since the symptoms were similar to scalenus anticus syndrome. The author indicates that the proper treatment in such cases is probably conservative management until the fragment can be successfully removed.

Ribo Rius<sup>1025</sup> describes 1 case of fractured spine due to the spasm of tetanus.

Wetzel<sup>1026</sup> describes 1 case of "shoveler's disease" (fracture of the dorsal spinous processes) and discusses the medicolegal aspects, particularly in regard to employee compensation.

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1022. Boorstein, S. W.: Treatment of Compression Fracture of the Spine, *Am. J. Surg.* **71**:216-221 (Feb.) 1946.

1023. Christensen, L.: Infections of the Urinary Tract Following Spine Fractures, *Ugesk. f. læger* **107**:283-287 (April 5) 1945.

1024. Brage, D.: Traumatic Detachment of Transverse Apophysis of First Dorsal Vertebra, *Prensa méd. argent.* **33**:928-930 (May 3) 1946

1025. Ribo Rius, L.: Fracture of the Spine Due to Tetanus, *Med. clin., Barcelona* **6**:273-276 (April) 1946.

1026. Wetzel, E.: Shoveler's Disease Among Agricultural Workers, *Schweiz. med. Wchnschr.* **76**:990-991 (Sept. 28) 1946.



[ED. NOTE (W. G. S.).—None of these articles presents anything particularly new or original, but they give helpful suggestions for the treatment of these serious injuries, particularly fracture-dislocations of the cervical portion of the pine.]

#### INJURIES TO THE MANDIBLE AND ABOUT THE FACE

Giordanengo<sup>1027</sup> presents a general discussion of the causes, pathologic features, age range and diagnosis in luxation of the mandible. He describes the classic method of reduction by manipulation of the thumb within the patient's mouth.

Meade<sup>1028</sup> describes a case of fracture of the neck of the condyle, with displacement; treatment was by open reduction. The author describes in some detail his method of fixation with circumferential sutures, followed by fixation of the jaw with a block placed between the molar teeth and the incisors held together by rubber traction.

Clarkson, Wilson and Lawrie<sup>1029</sup> give a report on 1,000 cases of fracture of the mandible in which treatment was administered by a maxillofacial surgical unit of the British Army. Six hundred patients were returned to active duty. The authors stress the importance of early closure of facial wounds in order to expedite recovery and minimize scarring. They used various methods of fixation, all more or less successful, and suggested that different methods were indicated for the treatment of different conditions. Tracheotomy was necessary in 27 cases; the authors state the belief that it should be done more frequently. For grafting they recommend the use of cancellous bone rather than molded or model grafts of cortical bone.

[ED. NOTE (W. S. G.).—This is a satisfactory and comprehensive article, well worth further study.]

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1027. Giordanengo, G.: Luxations of the Mandible, *Minerva med.* **2**:282 (Sept. 29) 1942.

1028. Meade, H. S.: Dislocation of the Mandible, *Irish J. M. Sc.* **2**:98-99 (March) 1946.

1029. Clarkson, P.; Wilson, T. H. H., and Lawrie, R. S.: Treatment of Jaw and Face Casualties in the British Army, *Ann. Surg.* **123**:190-208 (Feb.) 1946.

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#### CORRECTION

The last sentence of the article "Precautions and Results in Gastrectomy," by Drs. Ward H. Eastman and Warren H. Cole (September issue, page 768), should read: "The highest number of deaths from any single complication occurred in leakage of the duodenal stump (3 deaths) and cardiac disease (3 deaths)."

## EFFECT OF VAGOTOMY ON GASTRIC SECRETION IN MAN AND EXPERIMENTAL ANIMALS

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THE PRESENCE of gastric secretory fibers in the vagus nerves and the activation of these nerves by conditioned and unconditioned reflexes involving the sight, odor, taste or thought of food were established by the classic researches of Pavlov and his associates. Pavlov considered the secretory fibers in the vagi to be the most important mode of activation of the gastric glands and was doubtful if gastric secretion could occur after these nerves had been divided. The work of numerous English and American physiologists has, however, subsequently demonstrated that an abundant secretion of gastric juice of normal composition can occur after complete vagotomy in experimental animals, and the mechanism of this secretion has been extensively studied. The contact of food substances with the mucosa of the stomach and intestine is thought to cause the elaboration of a chemical substance which is absorbed into the blood stream and stimulates the gastric glands to increased activity. The mucosa of the antrum of the stomach was thought by Edkins to be particularly important in this connection, and he believed that the gastric stimulant provided by the antrum mucosa in response to the stimulus of food was a hormone for which he suggested the name gastrin. While both nervous and chemical factors are now well recognized to play a role in the physiology of gastric secretion, the relative importance of these factors has not been investigated. The widespread use of chemical stimuli such as histamine and alcohol in studying gastric secretion in patients with ulcer has perhaps over-emphasized the importance of the humoral or chemical mechanism in the minds of many observers. It is difficult to subject gastric glands of man or intact animals to the stimulus of food and make a quantitative collection

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of the gastric secretory response. A fairly quantitative collection of the continuous gastric secretion in the empty stomach of man between meals, as at night, can be accomplished by means of the indwelling gastric tube combined with continuous suction. Data on the gastric secretion in response to the ingestion of food, for the most part, must be secured on experimental animals provided with a Pavlov pouch or with a totally isolated stomach.

The widespread employment of gastric vagotomy in the treatment of peptic ulcer and the probability that this procedure depends for its beneficial effect on a reduction in gastric secretion have made it important to determine the relative importance of nervous and chemical factors in the control of gastric secretion in health and disease. Questions that come to mind are the following: How much does complete division of the vagus nerves to the stomach decrease gastric secretion in normal animals and in patients with ulcer? Does a partial interruption of the secretory fibers to the stomach produce a partial decrease in the nervous phase of gastric secretion, or must the vagotomy be complete? The studies to be reported in this paper were conducted in an attempt to provide answers for these questions.

#### CLINICAL STUDIES

The work of the older clinicians demonstrated that most patients with duodenal ulcers secrete more gastric juice in response to a test meal than do normal persons. Intermittent aspiration of the gastric content in the intervals between meals likewise indicated that the continuous or basal secretion of gastric juice was usually increased in these patients. In 1942 study of the volume and acidity of the nocturnal gastric secretion in patients with ulcer by means of an intranasal gastric tube with continuous suction was introduced as a routine in this service, and as a substitute for the various types of test meals or of alcohol or histamine stimulation. In 1944<sup>1</sup> it was reported that an excessive continuous secretion of gastric juice occurred in patients with duodenal ulcer and that this was reduced to normal or subnormal values by complete vagotomy. The method used at present for collecting the twelve hour night secretion is as follows: The patient is prepared for the test by the use of a clear liquid diet for twelve hours in the pre-operative period and thirty-six to forty-eight hours in the postoperative period. At 8 o'clock in the evening a Levin tube is passed into the stomach, and, if feasible, the position of the tube checked fluoroscopically. Ideally, the tube should pass through the cardia of the stomach, lying flat on the lesser curvature without kinks, and should extend deep into the fundus just short of the angulus. When it is correctly placed

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1. Dragstedt, L. R.; Palmer, W. L.; Schafer, P. W., and Hodges, P. C.: *Gastroenterology* 3:450, 1944.

and is functioning properly, the stomach is completely aspirated and the tube connected with a continuous suction apparatus. Continuous gastric aspiration is maintained from 8:30 p. m. to 8:30 a. m. the following morning. In addition to determining the volume and free acidity of this fasting gastric secretion, we have calculated the twelve hour output of free hydrochloric acid, expressing the result in milliequivalents of hydrochloric acid. Since free acidity as expressed in clinical units is synonymous with milliequivalents per liter, the volume of gastric juice secreted expressed in liters multiplied by the free acidity in clinical units equals the milliequivalents of free hydrochloric acid secreted in the twelve hour period. This figure will be referred to as the hydrochloric acid output. Levin, Kirsner, Palmer and Butler<sup>2</sup> have recently reported on a series of normal persons in whom the twelve hour nocturnal

TABLE 1.—*Twelve Hour Night Gastric Secretions of 135 Patients with Ulcer and 33 Normal Persons*

Percentage of Patients		Volume in Cubic Centimeters													Average
		0	200	400	600	800	1,000	1,200	1,400	1,600	1,800	2,000	2,200	2,400	
Ulcer.....	..	2	6	18	16	28	11	9	6	1	2	1	..	..	1,085
Normal.....	6	21	31	27	9	6	..	..	..	..	..	..	..	..	581

Percentage of Patients		Free Acidity in Clinical Units												Average
		0	10	20	30	40	50	60	70	80	90	100	..	
Ulcer.....	..	6	12	9	11	14	21	13	8	4	2	..	..	55
Normal.....	21	15	18	22	12	3	3	3	..	3	..	..	..	31

Percentage of Patients		Hydrochloric Acid Output in Milliequivalents													Average
		0	10	20	30	40	50	60	70	80	90	100	110	120+	
Ulcer.....	..	2	7	11	13	12	12	10	7	9	6	5	6	..	60
Normal.....	43	33	9	6	..	6	..	..	..	3	..	..	..	..	18

gastric secretion has been determined in this quantitative fashion. Table 1 shows this group of normal persons compared with a series of 135 patients with duodenal ulcer. The average volume in the former was 581 cc. in twelve hours, while in the group with ulcer the average was 1,085 cc., approximately twice as great. The average free acidity in the normal persons was 31 clinical units, and in the group with ulcer it was 55 clinical units. When the hydrochloric acid output is calculated, the difference is more striking. The average normal hydrochloric acid output was 18 milliequivalents, while that in the group with ulcer was 60, a nearly fourfold difference. Eighty-five per cent of the patients with duodenal ulcer secreted more than 35 milliequivalents of hydrochloric acid in the twelve hour period, and 85 per cent of the normal persons secreted less than 35 milliequivalents.

2. Levin, E.; Kirsner, J. B.; Palmer, W. L., and Butler, C.: Nocturnal Gastric Secretion, Arch. Surg. 56:345 (March) 1948.

In addition, the twelve hour night gastric secretion was determined for 23 healthy inmates of the Illinois State Penitentiary. The results, as shown in table 2, have considerable interest, in that these subjects secreted nearly double the amount of hydrochloric acid that normal persons studied at this clinic secreted; their average output of hydrochloric acid in the twelve hour period was 30 milliequivalents, as compared with 18 milliequivalents in the normal group previously shown. It seems most likely that this increase in gastric secretion is neurogenic in origin and is related to the emotional tension and stress associated with imprison-

TABLE 2.—Average 12 Hour Night Gastric Secretion

	Number of Cases	Volume, Cc.	Free Acid, Clinical Units	Hydrochloric Acid Output, mEq.
Normal persons.....	33	581	31	18
Normal persons (in prison).....	23	621	44	30
Patients with duodenal ulcer (before vagotomy)	70	1,006	52	55
Patients with duodenal ulcer (after vagotomy)	70	521	22	11

TABLE 3.—Twelve Hour Night Gastric Secretion in 70 Patients Before and After Vagotomy

Volume in Cubic Centimeters															
Number of Patients	Range.....	0	200	400	600	800	1,000	1,200	1,400	1,600	1,800	2,000	2,200	2,400	Average
Preoperatively	0	0	4	14	17	17	6	6	2	2	1	1	0	1,006	
Postoperative.	6	22	17	14	7	3	1	0	0	0	0	0	0	521	
Free Acidity in Clinical Units															
Number of Patients	Range.....	0	10	20	30	40	50	60	70	80	90	100	Average		
Preoperatively	0	6	11	9	10	7	11	9	6	1	..	..	..	52	
Postoperative.	20	19	14	6	6	4	0	0	1	0	..	..	..	22	
Hydrochloric Acid Output in Milliequivalents															
Number of Patients	Range.....	0	10	20	30	40	50	60	70	80	90	100	110	120+	Average
Preoperatively	1	6	8	11	9	4	11	3	7	5	1	1	3	55	
Postoperative.	48	9	9	3	0	0	0	1	0	0	0	0	0	11	

ment. It is interesting that there seems to be a high incidence of duodenal ulcer in the prison population.

That vagotomy produces a profound reduction in gastric secretion in patients with ulcer has been clearly demonstrated in previous reports from this clinic.<sup>3</sup> In this study quantitative studies of nocturnal gastric secretion were made for 70 patients with duodenal ulcer on whom vagotomy was performed between Jan. 18, 1943, and March 1, 1947.

3. Dragstedt, L. R., and Schafer, P. W.: *Surgery* **17**:742, 1945. Thornton, T. F.; Storer, E. H., and Dragstedt, L. R.: *Supradiaphragmatic Section of Vagus Nerves*, J. A. M. A. **130**:764 (March 23) 1946. Dragstedt, L. R.; Harper, P. V., Jr.; Tovee, E. B., and Woodward, E. R.: *Ann. Surg.* **126**:687, 1947.

Vagotomy was carried out by either the transthoracic or the transabdominal approach, but no additional surgical procedure was used in any of these patients. As shown in table 2, before vagotomy the average twelve hour volume was 1,006 cc., the average free acidity 52 clinical units and the average hydrochloric acid output 55 milliequivalents. After vagotomy, the average twelve hour volume was 521 cc., the average free acidity 22 clinical units and the average hydrochloric acid output 11 milliequivalents, a fivefold reduction in secretion. Table 3 shows these results in more detailed form. Figure 1 shows graphically the change in hydrochloric acid output produced by vagotomy in these 70 patients. It is noteworthy that only 20 of the 70 patients had com-

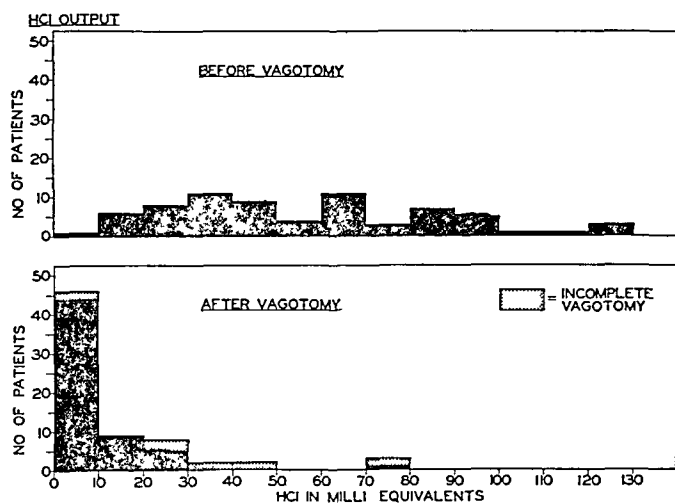


Fig. 1.—Twelve hour night gastric aspiration in 70 patients before and after vagotomy.

TABLE 4.—*Per Cent Reduction of 12 Hour Night Gastric Secretion in 70 Patients after Vagotomy*

	Volume										
Range.....	0	10	20	30	40	50	60	70	80	90	100
Number of patients.	4	4	8	7	7	10	14	10	6	0	Average 53%
	Free Acidity										
Range.....	0	10	20	30	40	50	60	70	80	90	100
Number of patients..	5	2	8	2	8	5	7	9	13	11	Average 61%
	Hydrochloric Acid Output										
Range.....	0	10	20	30	40	50	60	70	80	90	100
Number of patients..	4	1	0	0	4	6	6	7	10	32	Average 76%

plete anacidity of the fasting twelve hour night secretion after vagotomy. It is interesting to compare the secretion of the vagotomized patients with that of normal persons (table 2). It is apparent that vagotomy

has reduced the fasting nocturnal secretion in these 70 patients with duodenal ulcer to normal or subnormal levels. Table 4 shows the per cent reduction in the twelve hour night gastric secretion produced by vagotomy. The average reduction in volume has been 53 per cent, in free acidity 61 per cent and in hydrochloric acid output 76 per cent. Figure 2 shows the same data graphically. In 87 per cent of cases there has been more than a 50 per cent reduction in hydrochloric acid output, and in 60 per cent there has been a reduction of over 80 per cent.

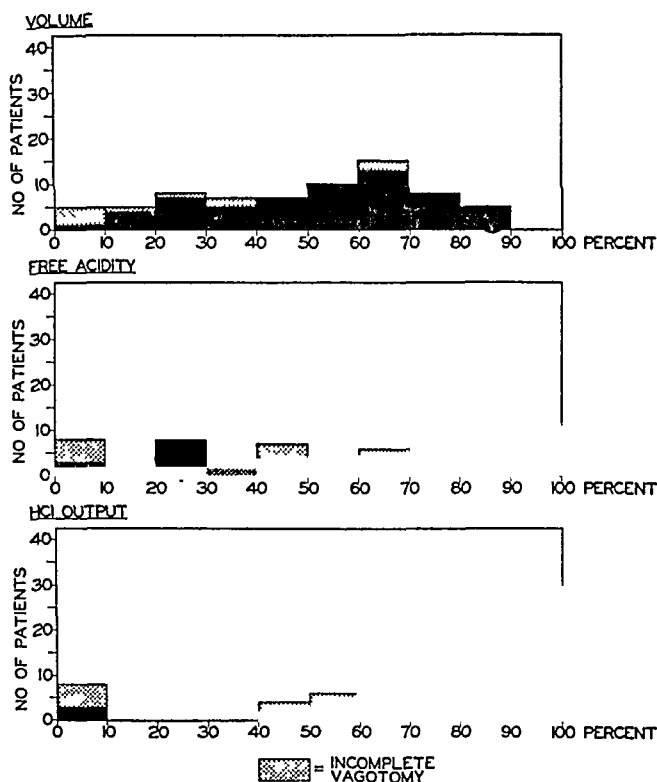


Fig. 2.—Per cent reduction of twelve hour night gastric secretion in 70 patients after vagotomy.

#### GASTRIC SECRETORY RESPONSE TO INSULIN HYPOGLYCEMIA: THE INSULIN TEST

The introduction of vagotomy as a clinical procedure has led directly to the development of clinical tests designed to evaluate the completeness and efficacy of the interruption of the vagal nervous pathways to the stomach. Vagotomy has been shown in the foregoing discussion to be most effective in reducing the acid secretion of the stomach of patients with duodenal ulcer in the absence of food or chemical stimuli. Historically this is the first clinical use of this effect in determining the completeness of vagotomy, and this test has been supplemented but not

supplanted by two other physiologic tests, the sham meal and the insulin test. The sham meal, which stems directly from the work of Pavlov, consists of exposing the patient to the sight, odor and taste of food under controlled conditions, while aspirating the stomach continuously with a Levine tube. To the best of our knowledge, this procedure has not been previously used as a clinical test except as reported from this clinic. The insulin test is based on the original observation of Bulatao and Carlson<sup>4</sup> that insulin hypoglycemia produced gastric hypermotility in dogs. This observation was confirmed and extended by other workers. The gastric hypermotility was found to be accompanied with hypersecretion of highly acid gastric juice rich in pepsin, and the effect was shown to be due to hypoglycemia and to be mediated through the vagus nerves.

The gastric secretory response to insulin hypoglycemia was used as a clinical test by Ihre<sup>5</sup> and Welin and Frisk<sup>6</sup> in Sweden in a manner similar to the use of the histamine test. Jemerin, Hollander and Weinstein<sup>7</sup> used the phenomenon to demonstrate the presence or absence of vagal innervation in the various types of gastric pouches in dogs, and Hollander suggested its use after vagotomy to determine whether or not the vagal pathways were in fact interrupted. It is the purpose of the present discussion to describe in detail the technics of these various tests as they are used in this clinic, point out the numerous pitfalls to which they are subject and which must be considered in evaluating each test and finally to correlate the results of the various tests, as well as our data permit, with the clinical findings.

The technic of the twelve hour night secretion study has been previously described. The insulin test or sham meal is generally used after this procedure with the help of the same Levin tube to which the patient has, by this time, become well accustomed. Placing of the tube is of great importance; this is usually best done under fluoroscopic control. The tip of the Levin tube should reach about the middle of the body of the stomach. If the tube is too far down, it may pass into the duodenum or through the gastroenterostomy stoma if one is present, thus vitiating the results of the test. Furthermore, a tube placed low in the stomach will be much more likely to collect samples contaminated with regurgitated bile or intestinal content, rendering the results of the test more difficult to interpret. Continuous aspiration is maintained

4. Bulatao, E., and Carlson, A. J.: *Am. J. Physiol.* **68**:148, 1924 and **69**:107, 1924.

5. Ihre, B. J. E.: *Human Gastric Secretion*, New York, Oxford Medical Publications, 1939.

6. Welin, G., and Frisk, R.: *Acta med. Scandinav.* **90**:543, 1936.

7. Jemerin, E. E.; Hollander, F., and Weinstein, V. A.: *Gastroenterology* **1**:500, 1943.



throughout the test with a glass or rubber bulb syringe. Usually this presents no problem, but not infrequently it is difficult to obtain adequate secretion for titration if the patient is not secreting well or if the Levin tube becomes occluded with food particles or folds of mucosa. Introduction of a small amount (20 to 30 cc.) of air through the tube and causing the patient to alter his position will almost always obviate these difficulties. Occasionally it is even possible to observe a periodic obstruction of the Levin tube caused by gastric contractions. A necessary step to avoid plugging of the tube with food particles during aspiration is to place the patient on a clear liquid diet for at least twelve hours before the test in a patient preoperatively and thirty-six to forty-eight hours, if possible, in a patient postoperatively. Samples are collected at ten minute intervals and placed in separate specimen bottles, and the character and color of the secretion are recorded. The volume of each sample is measured, and the free acidity is titrated with the use of Toeffer's reagent as an indicator. Samples heavily stained with bile must be properly evaluated when the results of the test are being interpreted. Contamination of the samples with saliva is minimized by instructing the patient to expectorate during the test and not to swallow any of his salivary secretion. After the first ten minute sample, a blood specimen is drawn for glucose determination, and 20 units of crystalline insulin is injected intravenously. The test is continued until a definite secretory response is observed, or for a period of ninety minutes following the injection of the insulin. The patient is carefully observed, and the symptoms of hypoglycemia are recorded. These occur in thirty-five to sixty minutes and may be very mild and transient or marked, although in our whole series of over 500 patients, most of whom have had two or more insulin tests, we have never had any untoward sequelae from the procedure. Only in patients with suspected coronary disease do we hesitate to use the test. We have never observed the occurrence of a gastric secretory response in the absence of hypoglycemic symptoms, although the reverse is occasionally true, even in the nonvagotomized subject. One hour after the injection of insulin, another blood sample is drawn for glucose determination. In choosing one hour as the interval, we were influenced by observations on a series of 87 patients at the Illinois State Penitentiary, on whom blood sugar determinations were done at thirty minute intervals for one and a half hours following the intravenous injection of 20 units of crystalline insulin. Glucose determinations were done on finger tip blood by the micro method of Folin and Malmros. This method gives figures that are somewhat high. The average fasting blood glucose level in this group of patients was 95.5 mg. per hundred cubic centimeters. Thirty minutes after the intravenous injection of insulin, the average blood glucose level was 49.0 mg., at sixty minutes it was 50.7 mg., and

at ninety minutes it was 53.6 mg. per hundred cubic centimeters. We feel that one hour allows sufficient time for the blood sugar to fall to its lowest point in the more resistant subjects, and in the patients with a more labile response the level has not begun to rise significantly at the end of a one hour interval. In an attempt to evaluate the necessary degree of hypoglycemia to produce a gastric secretory response, a careful analysis was made of fifty insulin tests in which a definite gastric secretory response was obtained. These are shown graphically in figure 3. Blood sugar levels were determined before and one hour after injection of

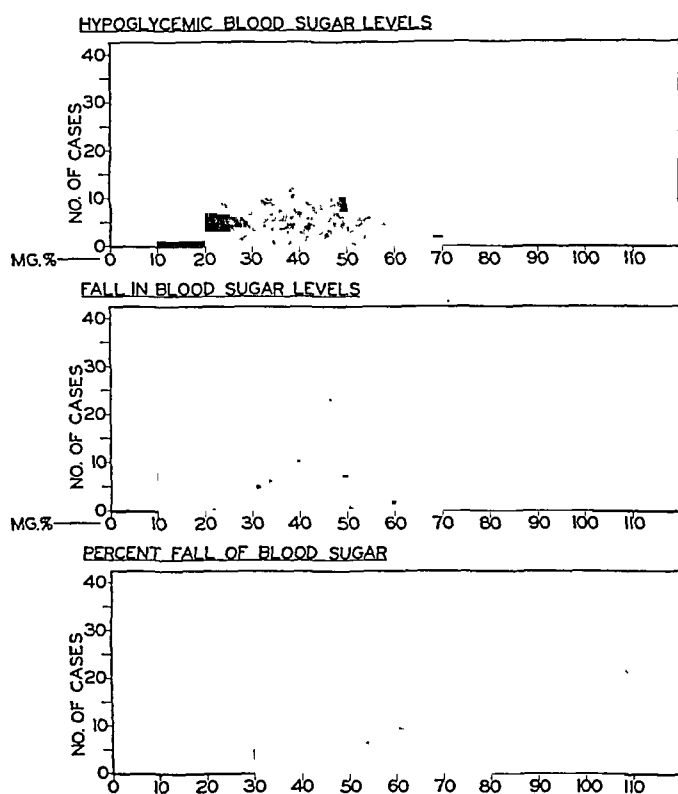


Fig. 3.—Observations on hypoglycemia in a series of 50 insulin tests which gave a positive reaction.

20 units of crystalline insulin intravenously, as described. They were determined photoelectrically, with the use of the Folin-Wu color reaction on the Shaffer-Hartmann filtrate. Inspection of the chart reveals considerable variation in both the degree of hypoglycemia and the actual fall in blood sugar, although the percentage fall shows a little more consistency. On the whole, we feel that the appearance of clinical signs and symptoms of hypoglycemia is probably a more constant and reliable criterion than the blood sugar level. The gastric secretory response occurs coincidentally with the hypoglycemic symptoms. In the presence of this response the test reveals vagal innervation to the stomach. Rarely,

for no known reason, with adequate lowering of the blood sugar and marked symptoms of hypoglycemia the secretory response is absent even in the presence of intact vagi. In all cases in which this has been encountered, repeated testing has resulted in a positive response. Occasionally the response is somewhat delayed, occurring fifteen or twenty minutes after the onset of hypoglycemic symptoms. In the

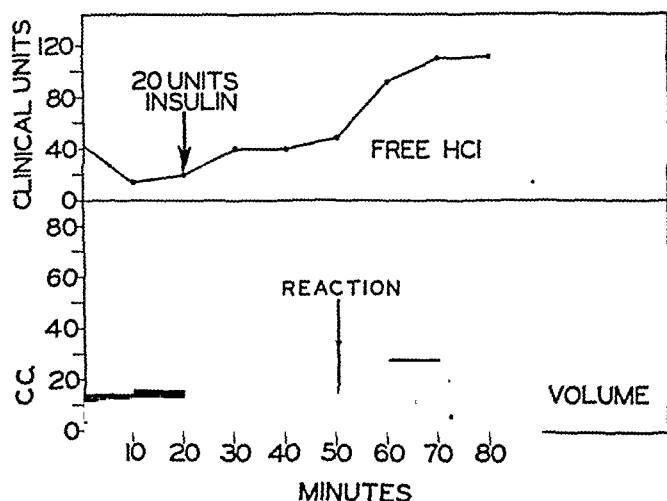


Fig. 4.—Positive gastric secretory response to insulin hypoglycemia.

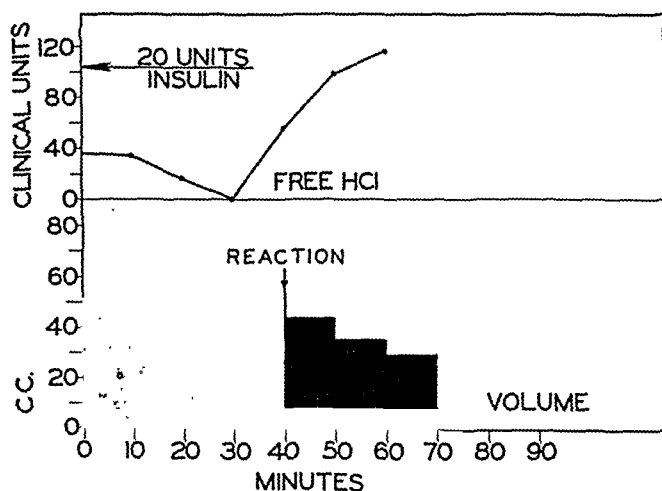


Fig. 5.—Positive (biphasic) gastric secretory response to insulin hypoglycemia.

normal reaction to the insulin test there is an increase in the volume and free acidity of the gastric juice (fig. 4). In almost half (42 per cent) of the tests there is observed a period of inhibition of secretion in which both the volume and the acidity of the aspirated gastric juice are much reduced (fig. 5). This period of inhibition occurs just before the onset of hypoglycemic symptoms. Its cause and mechanism are unknown. It seems to be unrelated to vagus function and as it is observed after vagotomy

(fig. 6). Even when the initial secretory level is high, the inhibitory phase may be observed followed by the normal secretory response (fig. 5). Occasionally there is no change in acid concentration, but a large volume of gastric juice is secreted during hypoglycemia. If reflux of intestinal content and technical errors in aspiration can be ruled out, this constitutes a positive response. A negative reaction to the test is characterized by the absence of the secretory increase coincident with the hypoglycemic symptoms. The secretory rate may stay the same or show a steady decrease or considerable inhibition. Indeterminate reactions are those in which there is continuous secretion at so high a level that any response would be obscured, and these are seen only preoperatively. Likewise, if there is no free acid in any sample, it is difficult sometimes to be sure that the test is valid, as the tube may

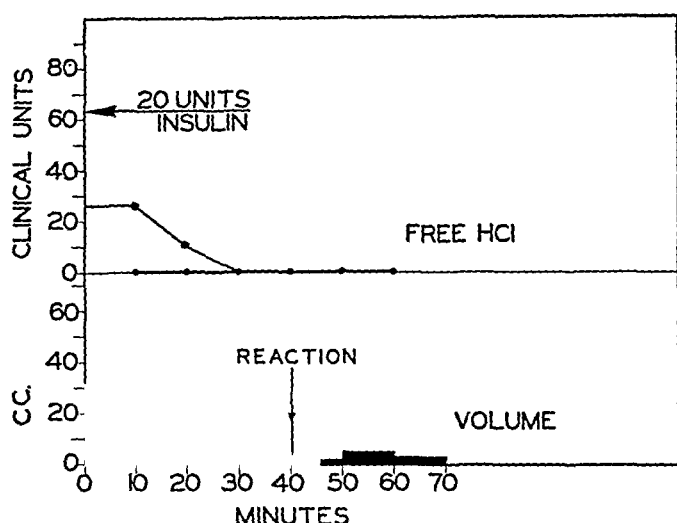


Fig. 6.—Negative reaction to insulin test following vagotomy, showing persistence of inhibitory phase.

have been displaced into the duodenum or jejunum or the samples may be contaminated by reflux of intestinal content. If these factors can be ruled out, such a reaction may be safely considered negative.

In view of the numerous complicating factors involved and the all-or-none (qualitative) nature of the test, we cannot set up arbitrary criteria for a positive response. Our own feeling, based on considerable experience, is that any reaction which raises doubt in the mind of the clinician who is attempting to evaluate it is probably positive and will prove so on subsequent testing.

The gastric secretory response to sham feeding is much less clear-cut than the response to insulin hypoglycemia, but it is nevertheless a useful confirmatory measure. When the insulin test is believed to be contraindicated, as in coronary disease, the sham meal may be used as

a substitute. The technic of collecting samples is the same as in the insulin test and is subject to the same difficulties. Three or four fasting ten minute samples are secured, and then the patient is presented with a light breakfast of his own choice, which he masticates and expectorates completely. Great care must be used to have the manner of presentation of the food as pleasant and appetizing as possible. The expectorated food must be disposed of rapidly and the container kept covered as much of the time as possible to avoid producing a feeling of disgust in the patient which results in a psychic inhibition of secretion. Unfortunately, it is almost impossible for most patients to avoid swallowing a little food and saliva, which results in partial neutralization of the gastric content as well as difficulty with aspiration of food particles. In our experience, only those who chew tobacco were able to undergo perfectly

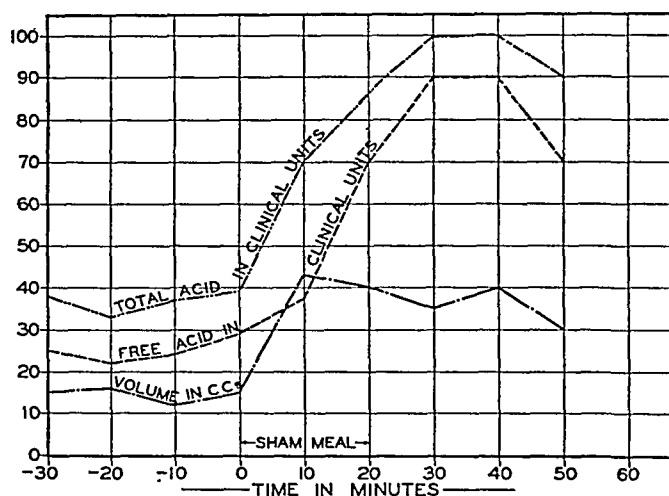


Fig. 7.—Typical gastric secretory response to sham feeding.

satisfactory sham meal tests. The period of mastication is allowed to continue for ten minutes, and samples are collected for the succeeding forty minutes. A positive response consists of a definite increase of secretion during the two samples following the termination of the meal (fig. 7). An increase in secretion occurring later than this is considered probably to be due to hormonal stimulation resulting from swallowed food particles. A comparison of the efficiency of the sham meal and the insulin test as a means of stimulating vagal gastric secretion is shown in table 5. It is obvious that insulin hypoglycemia is a much more efficient stimulus of gastric secretion than sham feeding and hence provides a more standard and reliable method of physiologic testing.

In reviewing the results of these various secretion studies in patients after vagotomy, it is apparent that between 10 and 15 per cent still have evidence of vagal pathways to the stomach. We consider these patients

to have undergone incomplete vagotomy. This incidence is proportionately the same in patients operated on transthoracically or by the transabdominal route. In a patient who shows a positive gastric secretory response with the onset of insulin-induced hypoglycemia, there seems

TABLE 5.—*Gastric Secretory Response*

Insulin Hypoglycemia		Sham Feeding
107 (100%)	Total Cases	45 (100%)
98 (92%)	Positive response	34 (76%)
1 (1%)	Indeterminate	1 (2%)
8 (7%)	Negative	9 (25%)
102 (96%)	Positive on repeated testing	36 (80%)

TABLE 6.—*Patients with Positive Reactions to Postoperative Insulin Tests After Incomplete Vagotomy\**

Number of Patient	Date of Operation	Operation	Reduction of Hydro- chloric Acid Output, %	Symptoms of Stasis	Clinical Results
11	5/24/44	Transthoracic vagotomy	27	0	Excellent
17	11/24/44	Transthoracic vagotomy	66	0	Excellent
22	12/27/44	Transthoracic vagotomy	None	++	Recurrence
28	1/19/45	Subdiaphragmatic vagotomy and posterior gastroenterostomy	45	0	Excellent
29	1/19/45	Subdiaphragmatic vagotomy and posterior gastroenterostomy	61	0	Recurrence
40	8/24/45	Subdiaphragmatic vagotomy	14	+	Recurrence
42	9/10/45	Transthoracic vagotomy	None	+++	Recurrence
46	11/ 7/45	Subdiaphragmatic vagotomy and posterior gastroenterostomy	None	0	Excellent
58	2/15/46	Subdiaphragmatic vagotomy and posterior gastroenterostomy	22	0	Excellent
59	2/27/46	Transthoracic vagotomy	..	++	Excellent
86	6/17/46	Subdiaphragmatic vagotomy and posterior gastroenterostomy	..	0	Excellent
88	6/24/46	Subdiaphragmatic vagotomy and posterior gastroenterostomy	..	0	Excellent
95	7/16/46	Subdiaphragmatic vagotomy and posterior gastroenterostomy	..	0	Excellent
116	9/24/46	Subdiaphragmatic vagotomy	57	0	Excellent
119	10/ 4/46	Subdiaphragmatic vagotomy and posterior gastroenterostomy	..	0	Excellent
124	10/18/46	Subdiaphragmatic vagotomy	None	0	Recurrence
X-2	10/17/46	Subdiaphragmatic vagotomy	..	++++	Excellent
X-10	12/ 5/46	Subdiaphragmatic vagotomy	..	0	Excellent

\* The diagnosis for patient 17 was jejunal ulcer. For all others it was duodenal ulcer.

little doubt that vagal innervation to the stomach persists. Consequently, we have used this criterion as our primary method of classification. In one series of 70 patients with duodenal ulcer treated by simple vagotomy, 10, or 14 per cent, had a positive insulin response after vagotomy. Correlation of the night secretion data with a positive postoperative insulin test in this group is shown in figure 1. Patients with

positive postoperative responses to the insulin test are designated in the crosshatched areas. In general, these patients have persistently high nocturnal gastric secretion postoperatively. Figure 6 shows that no patient with greater than 60 per cent reduction in his twelve hour night gastric secretion had a positive postoperative response to insulin. Conversely, of 18 patients who had less than 60 per cent reduction in the twelve hour night secretion, only 8 gave a negative response to the test. There is a small group of patients, who although they have persistently negative reactions to insulin tests, maintain a continued high night secretion. Three patients in this series of 70 demonstrated this phenomenon. Whether or not these patients have persistent vagal innervation to the stomach is a matter which is not as yet entirely clear. Among 160 consecutive patients treated by vagotomy 18 were found to have undergone incomplete vagotomy as defined previously. The clinical course of these 18 patients is summarized in table 6. One third of these patients have had persistence or recurrence of peptic ulcer.

#### EXPERIMENTS ON ANIMALS

Quantitative studies of the effect of vagotomy on the total secretion of gastric juice both in the fasting stomach and after the stimulus of food taking are almost necessarily inaccurate in man. The difficulties in collection led to the development in this laboratory of water-tight gastric fistulas which make possible quantitative collections of gastric juice from Pavlov or Heidenhain pouches or from the totally isolated stomach in animals for periods of many months. The production of the totally isolated stomach with preservation of its vagal innervation and blood supply was first described by Dragstedt and Ellis<sup>8</sup> in 1929, and the various modifications in the procedure in use in this laboratory at the present time are described in a recent publication.<sup>9</sup> This method lends itself admirably to a quantitative study of the effect of vagotomy since the total secretion of gastric juice by the isolated stomach may be collected for long periods before and after division of the vagus nerves to the stomach. The response of the stomach to insulin hypoglycemia makes it possible to check the functional capacity of the secretory fibers in the vagi before vagotomy and the completeness of this operation afterward.

Seventeen dogs were prepared with total isolation of the stomach as indicated in figure 8. After recovery from the operation, the gastric juice was collected in a rubber football bladder attached to the gold-plated brass or nylon plastic cannula. Each day the bag was emptied, the dog was given an intravenous infusion of Ringer's solution amounting to 100 to 200 cc. more than the previous twenty-four volume

8. Dragstedt, L. R., and Ellis, J. C.: *Am. J. Physiol.* **93**:407, 1930.

9. Dragstedt, L. R.; Woodward, E. R.; Neal, W. B., Jr.; Harper, P. V., Jr., and Storer, E. H., *Arch. Surg.*, to be published.

of gastric juice and the animal fed a standard diet of milk, sugar, horse-meat, hamburger, bone meal and brewer's yeast. Free acidity of the twenty-four specimen was determined by titrating with one-tenth normal sodium hydroxide, Toeffler's reagent being used as an indicator. Peptic power was determined by a method described by LeVeen.<sup>10</sup> A 1:250 dilution of gastric juice in 0.05 normal hydrochloric acid is incubated with a standard solution of egg albumin. The remaining albumin is precipitated with sulfosalicylic acid and determined nephelometrically on the Evelyn colorimeter.

Vagotomy was performed in 12 of the 17 animals, by the trans-thoracic route in 11 and transabdominally in 1. The figures for the twenty-four gastric secretion before and after vagotomy are summarized in table 7. In every case there was a profound reduction in the volume,

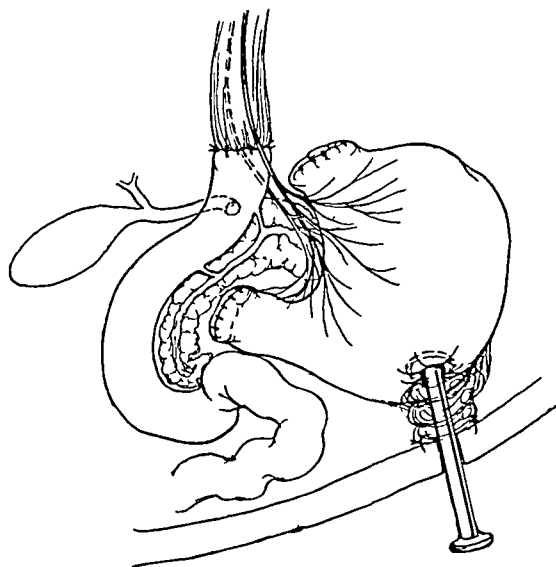


Fig. 8.—Diagram of the vagally innervated, totally isolated stomach in the dog.

free acidity and hydrochloric acid content of the twenty-four hour secretion as a result of the vagotomy. Table 8 shows the per cent reduction of the twenty-four hour secretion. The decrease in volume varied from 37 to 78 per cent, averaging 56 per cent. The decrease in free acidity of the twenty-four hour secretion varied from 18 to 82 per cent, averaging 49 per cent. The reduction in the twenty-four hour hydrochloric acid output varied from 46 to 92 per cent, averaging 76 per cent. This compares closely with the reduction obtained by vagotomy in the patient with duodenal ulcer. In 11 of the 12 animals, vagotomy produced a moderate decrease in the peptic power of the gastric juice. This reduction varied from 11 to 72 per cent, averaging

10. LeVeen, H. H.: *Proc. Soc. Exper. Biol. & Med.* 63:257, 1946.



TABLE 7.—*Effect of Vagotomy on Gastric Secretion in Total Pouch Dogs*

Dog No.	Before Vagotomy					After Vagotomy					Comments
	Number of 24 Hour Collections	Average Volume, Cc.	Average Free Acid, Clinical Units	Average Hydrochloric Acid Output, mEq.	Average Peptic Power, Units	Number of 24 Hour Collections	Average Volume, Cc.	Average Free Acid, Clinical Units	Average Hydrochloric Acid Output, mEq.	Average Peptic Power, Units	
D-802	19	1084	..	....	..	5	239	..	...	..	Died of perforated ulcer on 6th day after vagotomy
D-804	4	491	..	....	..	..	...	..	...	..	Died of perforated ulcer on 7th day
D-806	25	451	53	23.8	87	13	106	18	1.9	66	
D-812	10	802	72	58	84	16	355	17	6	59	
D-814	0	...	..	....	..	..	...	..	...	..	Died of perforated ulcer on 4th day
D-835	37	261	28	7.3	..	..	...	..	...	..	Persistently negative reaction to insulin test; vagi intact at autopsy
D-839	21	662	51	34	43	5	265	17	4.5	63	
D-861	7	604	35	21.1	80	2	243	16	3.9	48	
D-865	10	903	101	92	68	51	546	73	40	48	
D-875	17	756	109	82	88	35	358	59	21	25	
D-898	25	415	49	20	76	13	211	9	2	53	
D-912	30	331	71	24	88	43	210	61	13	78	
D-954	46	465	107	50.8	85	87	251	88	22.7	57	
D-962	87	441	100	44.1	88	230	111	57	8.3	65	Still living
D-979	33	834	105	87.6	104	..	...	..	...	..	Died in 6 weeks due to chronic hemorrhage from ulcer
D-996	45	624	94	58.7	..	39	304	60	15.2	..	Died of inanition; chronic ulcer in pouch
D-16	24	687	72	49.5	..	..	...	..	...	..	Died in 5 weeks due to chronic hemorrhage from ulcer

TABLE 8.—*Per Cent Reduction in Average Twenty-Four Hour Gastric Secretion Following Vagotomy in Total Pouch Dogs*

Dog Number	Hydrochloric Acid			
	Volume, Percentage	Free Acid, Percentage	Output, Percentage	Power, Percentage
D-802.....	78	..	..	..
D-806.....	77	66	92	24
D-812.....	56	76	90	30
D-839.....	60	67	87	47% increase
D-861.....	60	54	85	40
D-865.....	40	28	57	29
D-875.....	53	46	74	72
D-898.....	42	82	90	30
D-912.....	37	14	46	11
D-954.....	46	18	55	33
D-962.....	75	43	81	23
D-996.....	51	47	74	..
Average reduction.....	56	49	76	32

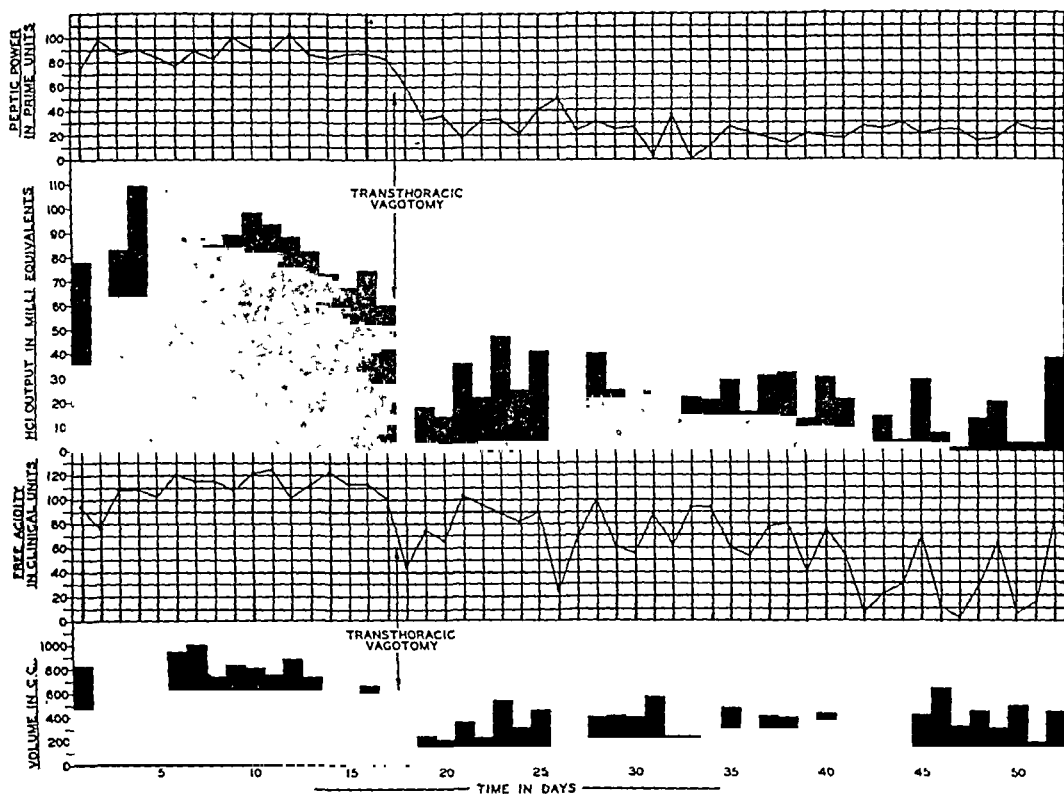


Fig. 9.—The effect of vagotomy on the secretion of the totally isolated stomach of dog 875. Daily twenty-four hour secretion.

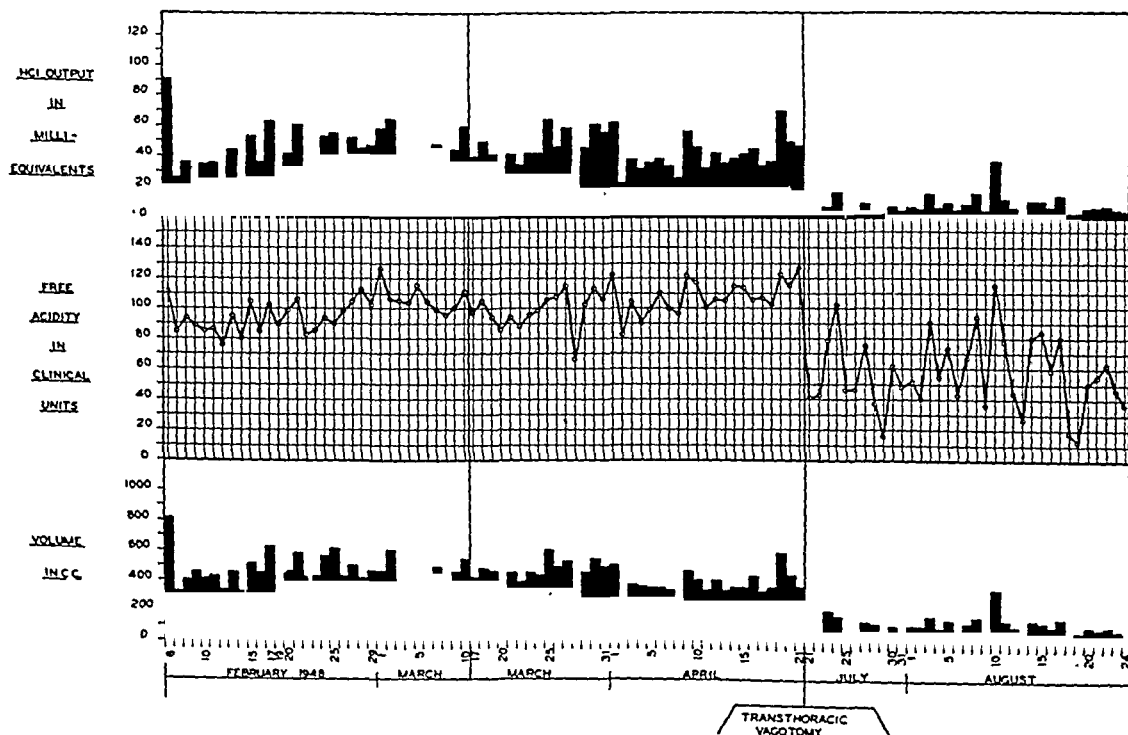


Fig. 10.—The effect of vagotomy on the secretion of the totally isolated stomach of dog 962. Daily twenty-four hour secretion.

32 per cent. In 1 animal, however, there was a 47 per cent increase in the peptic power of the gastric juice. Figures 9 and 10 illustrate in graphic form the change in the volume, free acidity, hydrochloric acid output and peptic power of the twenty-four hour daily secretion in 2 of these animals.

In each animal the integrity of the vagus innervation to the gastric pouch was established prior to vagotomy by the use of the insulin test. Essentially the same technic was used as in patients with peptic ulcer, with the exception that 5 or 10 units of insulin is adequate. In animals with a totally isolated stomach there is usually a pronounced augmentation in the secretion of gastric juice with the onset of hypoglycemia. Not only do the volume and free acidity rise, but also the peptic power of the gastric juice increases markedly. This increase in pepsin concentration, characteristic of "vagus juice," is as diagnostic of a positive response as is the increase in volume and free acidity. In the human being, however, an increase in peptic power has been so inconstant as to be of no diagnostic aid in interpretation of insulin response. In 1 dog (D-835, table 7) the response to insulin hypoglycemia remained negative, although at autopsy the vagus nerves were grossly intact. It is interesting that this animal's twenty-four hour secretion remained extremely low. After vagotomy, at least two negative responses to insulin hypoglycemia were obtained in each test animal.

The quantitative response of these animals to a standard dose of histamine was reported by Oberhelman and Dragstedt<sup>11</sup> to be markedly reduced. This reduction in hydrochloric acid output varied from 61 to 77 per cent, averaging 69 per cent in the 4 animals tested.

In 2 animals the effect of partial vagotomy was studied. In 1 the left vagus nerve was crushed in the neck, and, as seen in figure 11, the twenty-four hour secretion of gastric juice continued undiminished, although the peptic power of the juice was slightly reduced. The animal still responded to insulin hypoglycemia in the same fashion as before unilateral cervical vagotomy. After complete transthoracic vagotomy, there was a profound reduction in the volume and acidity of gastric secretion, and the reaction to the insulin test became negative. In the second animal the right vagus nerve was crushed in the cervical region, and in this animal also there was no decrease in the volume or acidity of the twenty-four gastric secretion. The animal still responded to insulin hypoglycemia. Again after complete transthoracic vagotomy, there was a marked decrease in gastric secretion and the reaction to the insulin test became negative.

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11. Oberhelman, H. A., Jr., and Dragstedt, L. R.: *Proc. Soc. Exper. Biol. & Med.* 67:336, 1948.

Four animals succumbed to peptic ulcer in the early postoperative period, 2 from perforation and 2 from hemorrhage. In each case autopsy revealed a typical, large, penetrating, chronic peptic ulcer. In 1 animal (D-861) bloody gastric juice indicated the presence of an ulcer. Trans-thoracic vagotomy was performed, but the animal died of a perforation five days later. In another animal (D-996) transthoracic vagotomy was performed in similar circumstances. Bleeding markedly diminished, and the juice eventually became relatively clear. However, the animal succumbed to inanition six weeks later, and autopsy revealed a large, healing ulcer with the base extensively filled in with scar tissue.

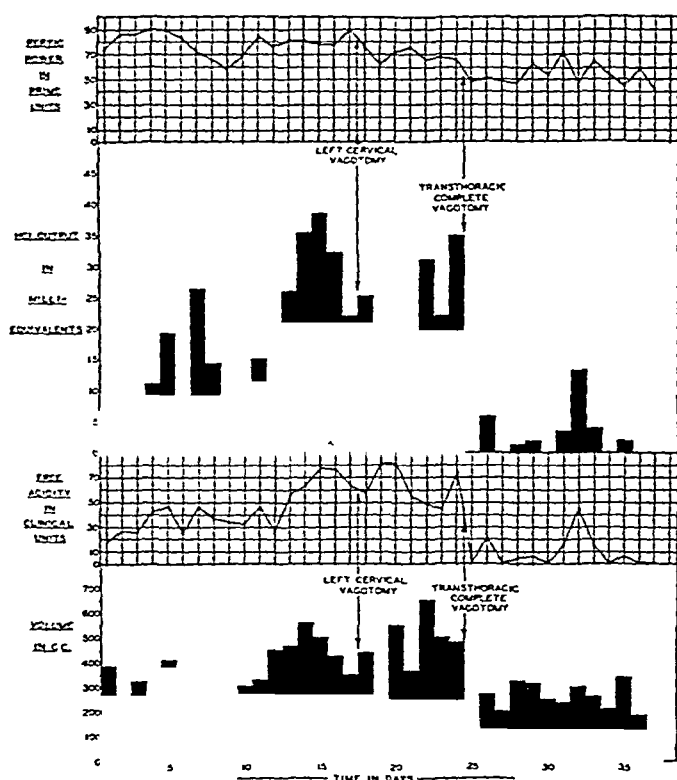


Fig. 11.—The effect of unilateral vagotomy on secretion of the totally isolated stomach of dog 898. Daily twenty-four hour secretion.

#### COMMENT

The regular occurrence of a continuous secretion of gastric juice in the intervals between meal taking in normal man may now be regarded as definitely established. This continuous secretion occurs at night during sleep and when the stomach has been completely emptied of food particles. It may be collected in large part by means of an accurately placed intranasal gastric tube combined with continuous suction. The volume of fluid obtained is of lessened significance since the specimens are often contaminated with swallowed saliva or regurgitated duodenal juices. If, however, measurements are made of the volume and the free

acid concentration, an estimation of the activity of the fundus glands may be obtained. The product of the two expressed as milliequivalents of hydrochloric acid represents the amount of acid secreted in the twelve hour period. It is probable that a measurement of the total chloride concentration would be more accurate since most of the chloride in the gastric content comes from the parietal cells. Normal adults were found to secrete an average of 18 milliequivalents of hydrochloric acid in the empty stomach at night when asleep and consequently shielded from the stimulus of food. Under the same conditions a series of 135 patients with duodenal ulcers secreted 60 milliequivalents, or almost four times as much. This excessive secretion is of neurogenic origin since in almost every instance it was reduced to considerably less than normal values by complete gastric vagotomy. In rare instances we have observed a persistence of hypersecretion in spite of what appeared to be a complete vagotomy, and these exceptional cases are the subject of further study. In a series of 70 patients the output of acid before operation was 55 milliequivalents, and this fell to an average of 11 milliequivalents after complete vagotomy. It thus appears that the continuous secretion in patients with duodenal ulcer is 80 per cent neurogenic in origin and 20 per cent dependent on other factors. The fact that the secretion of acid in these patients after vagotomy was less than that found in normal persons not operated on indicates that tonic secretory impulses over the vagus nerves play a large role in the continuous secretion of gastric juice in normal man. It is a surprising phenomenon that this nervous secretion continues during deep sleep. The excessive activity in patients with ulcer is probably in some way dependent on the nervous and emotional tensions so common among them, and this problem should be extensively studied. If the excessive tonic secretory activity of the vagus nerves proves to be due to emotional tension, the night secretion of gastric juice might prove to be of value as an objective measurement of this mental process. Psychotherapy reported to be of value in patients with ulcer could then be checked by quantitative measurement.

Determination of whether or not all the vagus fibers to the stomach have been interrupted remains an important factor in the postoperative check-up of patients undergoing vagotomy for peptic ulcer. Three criteria for this purpose are employed in this clinic at the present time. The most important of these is reduction in the output of acid in the night secretion. Failure to secure a reduction of more than 60 per cent usually means that the vagotomy has been incomplete. Second in importance is failure to demonstrate an increased gastric secretion in response to adequate insulin-induced hypoglycemia. The intravenous injection of 20 units of regular insulin usually suffices to reduce the blood sugar to about half the normal level and to produce hypoglycemic

symptoms. In our experience there is a better correlation between the appearance and severity of these symptoms and the degree of gastric secretory stimulation than obtains with the actual depression in the blood sugar level. The test is by no means infallible, and occasionally no increase in gastric secretion may be obtained in normal persons even with pronounced hypoglycemia and accompanying symptoms. When the test is repeated, however, a positive response is always secured. A persistently negative response may be obtained during the first two or three weeks after vagotomy even though all the vagus fibers have not been severed. This is probably due to trauma to these nerves at the time of operation. Recovery of their ability to conduct impulses is evidenced by a positive response to insulin hypoglycemia six weeks later. This immediate recovery must be interpreted not as indicating the regeneration of severed nerves but rather as a sign that the operation was incomplete.

Gastric secretory response to a sham meal as a test for persistent vagus function is at present employed only in patients in whom the production of insulin hypoglycemia may be contraindicated and as confirmation of the insulin test in doubtful cases. A positive response may be considered significant, but a negative result is meaningless unless secured in at least three tests.

The experiments on animals afford a degree of precision that cannot be secured in clinical studies, and here the great importance of the vagus nerves in gastric secretion is evident. The preparation used is not strictly physiologic, however, since only the nervous and intestinal phases of secretion are present. The antrum is in the isolated stomach, is shielded from contact with food and accordingly does not contribute its share in the total secretory stimulus of the food. The preparation permits, however, of a comparison of the relative importance of the nervous and intestinal phases of gastric secretion. After complete vagotomy the total output of hydrochloric acid from the stomach was reduced an average of 76 per cent, the volume 56 per cent, the free acidity 49 per cent and the peptic power 32 per cent. Thus, if the output of hydrochloric acid be taken as an index of the secretory activity of the fundus glands, the nervous phase of gastric secretion is more important than the intestinal phase in the ratio of 3 to 1.

The negative effect of unilateral vagotomy on gastric secretion is graphically illustrated in figure 11. In this animal with a totally isolated stomach, division of the left vagus nerve in the neck had no effect on the volume, free acidity or total output of acid in the gastric juice. A slight but possibly significant decrease in the output of pepsin was produced. This finding suggests that the individual vagus fibers do not innervate individual secretory cells or glands but rather that some intermediate plexus is involved.

## SUMMARY AND CONCLUSIONS

1. A continuous secretion of gastric juice occurs in normal persons when the upper part of the alimentary tract is empty of food and the subject is asleep or shielded from the sight, smell or taste of food. Under these conditions an average of 18 milliequivalents of hydrochloric acid is secreted during a twelve hour period at night.

2. Under the same conditions 135 patients with duodenal ulcers secreted an average of 60 milliequivalents of hydrochloric acid, or almost four times as much as the normal level.

3. The output of hydrochloric acid in patients with duodenal ulcer is reduced to an amount below the normal level by complete vagotomy, thus indicating that the hypersecretion in these patients is neurogenic in origin and also that the continuous secretion in normal man is partly due to a secretory tonus in the vagus nerves.

4. A determination of the amount of hydrochloric acid secreted by the empty stomach of patients with ulcer in a given period is the most important index of the secretory abnormality in these patients and is the best guide in evaluating the completeness of vagotomy and the most useful measurement in subsequent management.

5. An increase in gastric secretion in response to insulin hypoglycemia constitutes definite evidence that functional secretory fibers to the stomach are present. Failure to secure a response in normal persons is occasionally seen and not infrequently in the immediate postoperative period even when vagotomy has been incomplete. Repeated tests at subsequent periods elicit positive responses in these persons.

6. Repeated negative secretory response to insulin hypoglycemia is good evidence that vagotomy has been complete, and a reduction in acid output greater than 60 per cent is usually found.

7. An increase in gastric secretion in response to a sham meal indicates that functional secretory nerves in the vagi are present, but a single negative response is of less value as a criterion of complete vagotomy than is a negative response to insulin hypoglycemia.

8. In dogs with vagally innervated totally isolated stomachs, complete vagotomy reduces the output of hydrochloric acid by an average of 76 per cent. Since the nervous and intestinal phases of gastric secretion alone are operative in these animals, it is evident that the nervous phase is more important than the intestinal phase in the ratio of 3 to 1.

9. Section of one vagus nerve in the neck has no effect on the volume or acidity of secretion in dogs with vagally innervated isolated stomach preparations.

## SIDE EFFECTS AND COMPLICATIONS OF SYMPATHECTOMY FOR HYPERTENSION

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THE LITERATURE contains reports of several thousand patients who have undergone various forms of sympathetic denervation for the relief of hypertensive vascular disease. A comparison of the various types of operative procedures employed has been made by us elsewhere.<sup>1</sup> In general, the majority of patients reported on have undergone resection of the sympathetic chain from the ninth thoracic through the second lumbar ganglion combined with bilateral resection of the splanchnic nerves. Although our operations, especially in the more severe cases, have recently tended to be more extensive, we have usually limited our resections to this extent. As our familiarity with this operation has grown, we have become aware of certain problems associated with it, which, while they are not of a magnitude to limit seriously the use of the operation, are of importance if the optimum results are to be obtained and if the procedure is to be kept from falling into disrepute. A careful study of operative complications is clearly indicated as an aid in evaluating the side effects and the risks of the operation and in pointing out the complications which are peculiar to the type of patient on whom it is performed. By this means morbidity and mortality rates can be reduced, and final results will be improved.

### PHYSIOLOGIC CHANGES FOLLOWING SYMPATHECTOMY

Although certain changes in bodily physiology are an unavoidable result of sympathectomy, not infrequently if such effects have not been adequately explained preoperatively to the patient, these changes will be felt by him to represent complications of the surgical procedure rather than the anticipated result. Admittedly, from the patient's standpoint these alterations in his bodily functions may be disconcerting or even temporarily disabling, but they represent the price which he has

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1. de Takats, G.; Julian, O. C., and Fowler, E. F.: *The Surgical Treatment of Hypertension, Surgery* 24:469 (Sept.) 1948.



to pay for control of a disease which kills more persons than cancer each year.<sup>2</sup>

*Postural Hypotension.*—Among the side effects postural hypotension with its associated symptoms is the cause of most complaints. Whether or not postoperative postural hypotension is necessary to the achievement of a satisfactory reduction in blood pressure has not as yet been adequately determined though this would appear to be the case.<sup>3</sup> It is likely that patients in whom the vasospastic element constitutes the main cause of their hypertension will be the patients whose splanchnic and peripheral vascular bed will be most enlarged after removal of the sympathetic tone in these regions and hence who will have the greatest orthostatic hypotension. On the contrary, patients in whom the dilatation of the vascular bed is limited by the presence of organic disease, i. e., arteriolar sclerosis, will necessarily have a

TABLE 1.—*Relationship of the Severity of Hypertension to the Postural Hypotension Produced by Surgical Intervention*

Hypertensive Group	No. of Cases	Average Preoperative Blood Pressure	Average Postoperative Blood Pressure	Postural Hypotension	Result
Group I (mild).....	17	158/96	136/87	76/41	Good
Group II (moderate).....	24	207/128	176/110	103/53	Fair
Group III.....	10	234/158	210/153	None	All dead in 12 mo.

proportionately less significant postural hypotension. In our experience, unless a satisfactory postural fall in blood pressure is obtained, we have failed to perform an adequate sympathectomy or the patient was one of the group for whom sympathectomy was preoperatively considered to be of doubtful value but on whom operation was carried out as a last resort (case 1). We have found only slight reduction in the blood pressure after removal of the sympathetic vessels on one side, which is partially explained by the fact that the abdominal splanchnic pool in a large measure receives a bilateral sympathetic innervation which prevents notable enlargement of the vascular bed until bilateral denervation has been carried out and by the fact that unilateral denervation of an extremity is usually adequately compensated for by vasoconstriction of the remaining nondenervated portions of the body. However, after bilateral denervation in suitable cases, vasoconstriction in the nondenervated portions of the body is insuffi-

2. de Takats, G.; Heyer, H. E., and Keeton, R. W.: The Surgical Approach to Hypertension, J. A. M. A. **118**:501-506 (Feb. 14) 1942.

3. (a) Palmer, R. S.: Medical Evaluation of the Surgical Treatment of Essential Hypertension, J. A. M. A. **134**:9-15 (May 3) 1947. (b) de Takats, G., and Gilbert, N. L.: The Emergency Treatment of Apoplexy, *ibid.* **136**:659-665 (March 6) 1948.

cient to compensate for the vastly enlarged vascular bed, and postural hypotension is the end result. It is usual for a sympathectomized patient to demonstrate marked postural hypotension during the first few weeks or even months unless supportive measures are instituted. Even so, a patient whose blood pressure has been considerably reduced will at least be uncomfortable and will usually complain of fatigue, weakness and mental lassitude. A convalescence free of disabling hypotensive symptoms will be a rapid and relatively pleasant one, but, in general, this does not augur well for satisfactory long term results.

The temporary dizziness, faintness and lack of mental acuity present postoperatively in these patients is due primarily to a diminished circulating blood volume, although compensatory vasoconstriction of the cerebral vessels which further accentuates the cerebral anemia may represent a minor factor. That some degree of cerebral vasoconstriction can be present would appear to be demonstrated by the observation that procaine hydrochloride block of the appropriate stellate ganglion after cerebral thrombosis will often in a few minutes produce improvement in both motor and sensory paralysis and in psychic depression.<sup>3b</sup> This explanation is also suggested by cases with latent cerebral damage in which this damage has regained prominence after operation presumably because of diminished cerebral circulation (case 2).

*Substernal Fluttering and Breathlessness.*—A majority of patients will note a sensation of substernal fluttering or breathlessness early in their postoperative course, though not to a degree that might suggest anginal pain. The sensation of substernal fluttering is due to acceleration in the pulse rate in an attempt by the heart to compensate for the sudden fall in blood pressure, which is the result of decreased venous return to the heart. As is well known, postural hypotension and its associated unpleasant symptoms can be obviated to a large degree if the patient will assume the standing position only gradually or if he will avoid standing still once the erect position has been attained, since in both situations venous return is poor because of pooling of blood in a fully opened vascular bed. Wrapping of the lower extremities with elastic bandages and the use of elastic hose combined with an elastic girdle may occasionally be required for a period of weeks for severely incapacitated patients.<sup>4</sup> Before many weeks or months have elapsed, however, this notable degree of hypotension will disappear; some degree of postural hypotension may persist for years but not to the point at which it is uncomfortable.

*Hyperhydrosis.*—Hyperhydrosis of the nondenervated portions of the body may be discomforting for the patient. This, too, is most

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4. Gambill, E. E.; Hines, E. A., and Adson, A. W.: The Effect of Certain Postures on Circulation Before and After Extensive Sympathectomies for Essential Hypertension, Proc. Staff Meet., Mayo Clin. 19:271-278 (May 31) 1944.

severe during the immediate postoperative period and either gradually diminishes or loses significance in the eyes of the patient. Persistent, profuse, uncontrollable diaphoresis of the nondenervated areas has occurred most often among patients who underwent nearly maximal sympathectomies. Excessive sweating of the head and the upper extremities in such cases has at times produced an annoying and socially undesirable situation. Recently, a remote possible complication of extensive denervation relative to the problem of sweating has come to our attention in the case of a man who, after sympathectomy, repaired to a tropical climate, where he was apparently susceptible to heat exhaustion presumably because of the inadequacy of his heat-dissipating mechanism due to reduced sweating ability. A residual sweating area around the waist at the twelfth dorsal dermatome is often present without any scoring influence on results.

*Accentuation of the Vasomotor Tonus.*—Compensatory accentuation of the vasomotor tonus of the nondenervated portions of the body may be manifested by notable alterations in the vascular supply of the upper part of the trunk and the upper extremities. The observation of some patients subjected to sympathectomy will disclose cold, bluish white, mottled extremities, which will suggest the presence of cutis marmorata, acrocyanosis or even Raynaud's disease, though actually this is merely a manifestation of varying degrees of compensatory vasoconstriction in response to homeostatic demands. Case 5 is illustrative of such a response. Moreover, no severe trophic disturbances or actual gangrene can occur in the absence of previously demonstrable local vascular damage in the affected areas.

*Derangement of Sexual Functions.*—This is a matter of importance to the younger hypertensive men. Despite numerous references in the literature to the fact that the removal of the first and second lumbar ganglions bilaterally will produce loss of libido, failure of ejaculation and even sterility,<sup>5</sup> this has not been uniformly the case in our experience<sup>6</sup> or in that of others.<sup>7</sup> It seems probable that other factors are often involved when impotence does occur. Because of the importance of the psychologic element in influencing libido and potency, we have felt it unwise to emphasize this occasional undesirable sequel to sympathectomy by special reference to it in our postoperative follow-up

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5. Simeone, F. A.: A Neuromuscular Mechanism in the Ductus Epididymidis and Its Impairment by Sympathetic Denervation, *Am. J. Physiol.* **103**:582-591 (March) 1933. Learmonth, J. R.: A Contribution to the Neurophysiology of the Urinary Bladder in Man, *Brain* **54**:147-176 (June) 1931.

6. de Takats, G., and Helfrich, L. S.: Sterility of the Male After Sympathectomy, *J. A. M. A.* **117**:20-21 (July 5) 1941.

7. Poppen, J. L., and Lemmon, C.: The Surgical Treatment of Hypertension, *J. A. M. A.* **134**:1-8 (May 3) 1947.

studies. Casual questioning or information volunteered by the patients has indicated no close correlation between the extent of denervation and sexual ability or libido. Erection has rarely been influenced; ejaculatory ability has more often been adversely affected. Sympathectomy has no adverse effect on the female genital tract since many records are available of women who, contrary to our advice, have become pregnant and have borne normal children. That an increase in blood supply to the reproductive organs may be at least a temporary result is suggested by 1 of our cases, in which a woman in whom menstruation had ceased a year prior to surgical intervention started to have regular periods in the absence of any demonstrable pelvic disease (case 4).

*Motor or Sensory Dysfunction.*—Motor or sensory dysfunction of a large portion of the intestinal tract might be anticipated as a result of its sympathetic denervation to a large degree. Postoperative abdominal discomfort and distention have not been rare in our experience, and it has been for this reason that we have avoided too rapid resumption of a general diet and have also felt it worth while to administer an ampule of neostigmine twice daily for the first few days. Distention and decreased intestinal motility is the reverse of what might be expected since the sympathetic supply to the bowel is largely inhibitory and the action of the now unopposed vagus is predominantly motor and secretory<sup>8</sup>; however, the degeneration of the residual preganglionic fibers might so stimulate the celiac ganglion cells that their postganglionic fibers might produce a transitory inhibitory effect on visceral motility. A subsequent increase in gastric motility and secretion might cause the development or recurrence of gastric or duodenal ulcers. This would appear to be a distinct possibility since autonomic instability is common to both the hypertensive person and the patient prone to suffer from ulcers. We have not noted this complication in our cases possibly because the concomitant alteration in visceral sensation may have masked the symptoms. Belgen and Kinter have reported cases in which there was aggravation of ulcer symptoms after sympathectomy,<sup>9</sup> and one of us (E. F. F.) has encountered a patient with reactivation of a previously healed ulcer as demonstrated by severe hemorrhage and enlargement of the ulcer crater, though in the absence of visceral pain, following sympathetic denervation. The recent work of Dennis; who has been employing vagotomy successfully in the alleviation of symptoms of ulcerative colitis, would by inference suggest that severe diarrhea or even ulceration of the bowel might be the occasional result

8. White, J. C., and Smithwick, R.: *The Autonomic Nervous System*, ed. 2, New York, The Macmillan Company, 1946, p. 137.

9. Belgen, H. M., and Kintner, A. R.: Aggravation of Gastric Ulcer Following Dorsolumbar Sympathectomy, *J. A. M. A.* **133**:1207-1208 (April 19) 1947.

of extensive sympathetic denervation, although this complication has not been reported. In fact, a spastic type of constipation seems to prevail.

*Elimination of Visceral Pain.*—Elimination of the sensation of visceral pain by sympathetic and splanchnic denervation has recently received much attention.<sup>10</sup> It has been known for years that gastric, renal, biliary and pancreatic pain as well as muscular rigidity of the abdominal wall due to reflex visceral action can be alleviated by sympathetic blocks of the seventh dorsal through the second lumbar segment and the selective blocking of definite levels has been utilized for differential diagnostic purposes.<sup>11</sup> Operations on the sympathetic nervous system directed toward the relief of intractable abdominal pain have been shown to be effective and are clearly indicated when further surgical intervention is contraindicated. However, the very success of these procedures serves to point out another possible complication inherent in sympathectomy for hypertension. Surgical removal of the visceral sympathetic nerve supply may so modify or abolish normal visceral sensation that the presence of ulcer or its complications, the acute manifestations of gallbladder, renal or pancreatic disease or, equally important, the development of malignant disease may be completely masked or misinterpreted until its late stages, when involvement of somatic nerves or systemic manifestations become evident. Time and careful post-operative observation of patients subjected to sympathectomy will determine whether or not these considerations are more theoretic than actual.

#### THE IMPORTANCE OF PROPER SELECTION OF CASES

Since not all cases of hypertension are amenable to surgical treatment, proper selection becomes a matter of vital importance if satisfactory results are to be obtained in a high percentage of cases and the incidence of complications is to be kept at a minimum. Our indications for surgical intervention have been discussed elsewhere,<sup>12</sup> but in brief they are based on the exclusion of patients whose hypertension is

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10. Bronson, R. S., and Neill, C. L.: Abdominal Visceral Sensation in Man, *Ann. Surg.* **126**:709-724 (Nov.) 1947. Grimson, K. S.; Hesser, F. H., and Kitchin, W. W.: Early Results of Transabdominal Coeliac and Superior Mesenteric Ganglionectomy, Vagotomy, or Transthoracic Splanchnicectomy in Patients with Chronic Abdominal Visceral Pain, *Surgery* **22**:230-239 (Aug.) 1947. de Takats, G., and Walter, L. E.: The Treatment of Pancreatic Pain by Splanchnic Nerve Section, *Surg., Gynec & Obst.* **85**:742-746 (Dec.) 1947.

11. de Takats, G.: *Local Anesthesia*, Philadelphia, W. B. Saunders Company, 1928.

12. de Takats, G.; Fowler, E. F.; Graupner, G. W., and Jensik, R. J.: The Surgical Approach to Hypertension: Second Report, *Arch. Surg.* **53**:111-163 (Aug.) 1946. de Takats, G., and Fowler, E. F.: The Surgical Treatment of Hypertension: III. The Neurogenic Versus Renal Hypertension from the Standpoint of Operability, *Surgery* **21**:773-799 (June) 1947.

attributable to renal disease such as polycystic kidney, hypoplastic kidney, urinary obstruction and acute nephritis. However, nephrosclerosis and hypertensive vascular disease may persist after elimination of unilateral renal disease by means of nephrectomy, and in such instances section of the splanchnic nerves has given us spectacular results. Other contraindications are conditions in which hypertension is a manifestation of endocrine imbalance, of which the commonest examples are hyperthyroidism, menopausal syndrome, adrenal tumor and pleuriglandular syndromes of pituitary origin; situations in which disease of the central nervous system is fundamental, i. e., conditions producing increased intracranial pressure and psychic conditions or neurogenic syndromes not mediated through the splanchnic nerves, and finally vascular lesions of congenital origin, of which coarctation of the aorta is representative, or of acquired origin such as cardiac failure from whatever cause or arteriosclerosis in which a rigid aorta combined with arteriolar sclerosis produces a picture of hypertension but not one which we feel is benefited by sympathectomy. The remaining cases of hypertension of the so-called essential type we have divided into three groups for purposes of analysis of operative results. Of these, we have been of the opinion that only groups I and II can be definitely said to be benefited by sympathectomy. We have not felt that the history of cerebral vascular accidents, coronary occlusion or moderately diminished renal function as evidenced by slight elevation of the blood nonprotein nitrogen level need necessarily constitute an absolute contraindication to surgical intervention since not a few of the patients with these conditions may receive benefit from sympathectomy, though such incidents will to some extent influence our selection of cases. Reluctantly we have operated on some patients in group III despite the poor prognosis which is offered with or without surgical treatment, but our results have as a rule borne out our gloomy attitude. We are aware that this is not the approach or the attitude of all workers in this field,<sup>13</sup> but we believe that our conservative attitude is responsible for our lower morbidity and mortality rates.

#### THE COMPLICATIONS OF SECTION OF THE SPLANCHNIC NERVES PER SE

A hypertensive patient is not normal, and since this is so, it is natural that there should be certain complications peculiar to or more frequently encountered in the surgical care of such patients. In cases

13. Smithwick, R. H.: The Surgical Treatment of Hypertension, *Arch. Surg.* **49**:180-193 (Sept.) 1944. Peet, M. M.; Woods, W. W., and Braden, S.: The Surgical Treatment for Hypertension: Results in Three Hundred and Fifty Consecutive Cases Treated by Bilateral Supradiaphragmatic Splanchnicectomy and Lower Dorsal Sympathetic Ganglionectomy, *J. A. M. A.* **115**:1875-1878 (Nov. 30) 1940.

of hypertension, particularly those of the most severe type, cardiac, cerebral or renal complications are prone to develop as a direct result of sudden lowering of the blood pressure to an unaccustomed level. Preliminary evaluation in such cases may have demonstrated varying degrees of damage to these systems due to prolonged exposure to elevated intravascular pressure, and this may be made clinically evident or, if already clinically evident, accentuated by the newly acquired level of blood pressure.

*Cardiac Complications.*—Although it has been recognized for several years that patients with hypertension subjected to sympathectomy usually obtain notable subjective relief from previous cardiac complaints and that objective improvement as evidenced by electrocardiographic changes and diminution of the size of the heart is frequent,<sup>14</sup> this is not uniformly the situation. The improvements which are noted are due to a lightening of the cardiac load which follows the decrease in the peripheral resistance of the now dilated vascular bed. This is not only desirable but is usually essential to a satisfactory operative result. Still, early in the postoperative period a rapid shifting of the circulating blood volume may so diminish venous return that cardiac failure may be precipitated unless adequate care is rapidly instituted. Case 2 will serve to illustrate this point. If the circulatory system is supported during this critical period, a later satisfactory adjustment of the heart to its new working conditions will gradually occur unless actual chronic coronary insufficiency has been produced. It is also conceivable that a temporary reduction in coronary blood flow combined with changes in blood coagulability in the postoperative period might predispose to the production of coronary thrombosis. This is a supposition, however, which is difficult to prove clinically since the subsection of a patient with an already damaged vascular system to operation is in itself hazardous because the cardiac load is thereby increased appreciably if only for a short period. Case 3, in which operation was performed on another service, serves as a possible illustration of a death due to coronary thrombosis precipitated by the load of operation or the physiologic changes wrought thereby.

*Cerebral Complications.*—We have encountered several examples of disturbed cerebral function of a localizing nature following sympathectomy which would appear to be explicable on a basis of decreased cerebral blood flow due either to relative cerebral anoxia or to small foci of cerebral thrombosis precipitated by surgical intervention. Of interest is the fact that previously unnoted neurologic disorders have

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14. Bridges, W. C.; Johnson, A. L.; Smithwick, R. H., and White, P. D.: Electrocardiography in Hypertension, *J. A. M. A.* **131**:1476-1480 (Aug. 31) 1946.

regained their former prominence for variable periods after operation. We have been fortunate in that these untoward manifestations have thus far been of a transitory nature though this might not always have been the case. Case 2 represents an example of this sort. Nonlocalizing manifestations of altered cerebral function such as psychic disturbances, usually mental depression or mental retardation, are not uncommon among the more severe cases of hypertension. We have had 1 case in which a definite psychosis developed postoperatively which was of extended duration.

*Renal Complications.*—Serious renal complications incident to surgical lowering of the blood pressure have not been notable in our series of over 250 cases, possibly because of our care in eliminating patients

TABLE 2.—*Surgical Complications of Sympathectomy for Hypertension in 100 Cases (i. e., 200 Operations)\**

Complications	No. of Cases	Incidence, %
A. Severe complications		
(1) Cardiac.....	6	3
(2) Neurologic.....	6	3
(3) Renal.....	0	0
(4) Shock.....	2	1
B. Painful complications		
(1) Mya'gia.....	10	5
(2) Neuralgia.....	16	8
C. Pulmonary complications		
(1) Pneumothorax and atelectasis (on roentgenologic examination) .....	28	14
(2) Hydrothorax or hemothorax (on roentgenologic examination) .....	18	9
D. Wound infection.....	4	2

\* The prolonged morbidity rate was below 10 per cent and the mortality rate below 1 per cent.

with severe renal damage. Still, it is theoretically possible that a situation might arise in which excessive lowering of the blood pressure might so diminish renal perfusion and glomerular filtration pressure that adequate excretion of waste products might be made impossible. This complication must be relatively infrequent even in kidneys damaged to the point where there is some increase of the nonprotein nitrogen level. A reduction in filtration pressure may even in some measure be compensated for by reduction in renal ischemia resulting from sympathetic denervation. Postoperative deaths due to uremia have, however, been reported by others,<sup>15</sup> exclusive of instances in which sympathectomy obviously failed to arrest progression of the hypertensive process.

15. Phelps, M. L., and Burdick, D. L.: Anesthetic Management of Patients Undergoing Sympathectomy for Hypertension, *Anesthesiology* 4:361-371 (July) 1943.



THE TECHNICAL COMPLICATIONS OF SECTION OF THE  
SPLANCHNIC NERVES

If proper selection of cases has been employed, technical complications will account for most of the morbidity encountered after sympathectomy.

*Shock.*—Shock should be a rare occurrence in any planned surgical procedure if proper precautions are taken. Particularly in hypertensive persons, prolonged periods of hypotension are undesirable not only because of the ease with which patients go into profound shock but also because of the increased dangers of the effect of hypoxia on the already damaged cerebral and cardiac systems. We believe that performance of a bilateral sympathectomy and splanchnic resection at a single operation is an unnecessarily hazardous undertaking from the standpoint of shock since it is more time consuming, it necessitates readjustment of the position of the anesthetized patient which predisposes to a fall in the blood pressure and it produces a more rapid alteration in the circulating blood volume. Even in the two stage operation, particularly during and after the second stage, it is necessary to be on guard against acute hypotension. Utilization of fluids intravenously, preferably blood, and the intravenous or intramuscular administration of phenylephrine hydrochloride (neo-synephrine hydrochloride®) are routinely employed to maintain blood volume and blood pressure. On the patient's return from surgery, 18 inch (45.7 cm.) shock blocks are placed beneath the foot of the bed to assist venous return and to minimize cerebral ischemia. If close observation in the postoperative period reveals shock to be present or imminent, in addition to the continued administration of fluids intravenously, oxygen is administered, elastic bandages are applied to the extremities and a snug abdominal binder is used to prevent hypoxia and to support blood volume (case 2). Control of pain is essential to the patient's comfort and will also militate against shock.

*Pulmonary Complications.*—Pulmonary complications are common and may be the result of certain technical errors or oversights. Pre-operative freedom of the patient from respiratory infections and adequate oral hygiene require no emphasis. To reduce bronchial secretion, which hampers anesthesia and predisposes to subsequent atelectasis, we utilize 1/150 grain (0.4 mg.) of atropine or 1/200 grain (0.3 mg.) of scopolamine prior to anesthesia. Good anesthesia is of extreme importance both to the general condition of the patient and in the provision of conditions favorable to rapid operation.<sup>16</sup> In this connection, we have found induction with nitrous oxide followed by ether most satisfactory. The

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16. Langston, H. T.: The Pathology of Chronic Hemothorax, *Surgery* **21**: 137 (Jan.) 1947.

technic of sympathectomy requires no elaboration, but we believe that there are definite advantages to be obtained from maintaining the pleura intact. The retropleural exposure and the identification of the sympathetic chain and the splanchnic nerves are not difficult, and if perforation of the pleura is avoided the immediate complications represented by a flapping mediastinum and by increased anesthetic difficulties are obviated and late complications such as pneumothorax, hemothorax or reactive hydrothorax are reduced. The pleura is most frequently damaged during one of the following steps: during subperiosteal removal of the rib, in cutting the rib at its costochondral junction anteriorly or at the costovertebral junction posteriorly, at which point the pleura is firmly adherent, or during pleural reflection from the thoracic wall if there has been a failure to reflect the endothoracic fascia with the pleura, the pleura alone being so fragile that it is impossible to maintain it intact. During section of the diaphragm, if the pleural reflection onto the diaphragm is not clearly visualized or if forcible retraction of the lung is attempted before the pleura has been well separated from the thoracic wall, tension on the pleura may tear it or so distort the cleavage planes that a pneumothorax is produced. Occasionally the mediastinal reflection of the pleura may be mistaken for the splanchnic nerve momentarily, and in the attempt to pick this up with a sympathectomy hook a perforation may be produced. If previous pleuritis or mediastinitis has left its mark with dense adhesions, it may be difficult to avoid pleural perforation; if this occurs, all air and blood must be removed from the pleural cavity at the completion of the surgical procedure.<sup>16a</sup> Before the patient leaves the operating room physical examination and, if necessary, thoracocentesis should demonstrate the absence of pneumothorax and of a significant degree of atelectasis. Compression of the lung during the surgical procedure as well as pleural perforation predisposes to atelectasis on the side operated on, though equally often the other side will be discovered to be atelectatic because of mediastinal shift and the gravitation of secretions to this side. A thorough endotracheal toilet and adequate pulmonary aeration are largely the responsibility of the anesthetist and are an important one. However, the good work of the anesthetist must not be nullified by binders which limit expansion of the chest, undue depression of the cough reflex by unsuitable analgesic agents or failure to relieve pain so that the patient will be willing to cough or the unnecessary use of oxygen which will reduce the amplitude of respiration. On the positive side, the intermittent use of carbon dioxide inhalations may be of some aid in dislodging residual mucous plugs by provoking coughing. We believe that the prophylactic use of peni-

16a. At present, when entered, all pleural cavities are drained with mushroom catheters and continuous suction is used for forty-eight hours.

cillin is indicated not only for the control of infection in residual atelectatic areas but also for the huge area of dissection which has been contaminated to some degree. Should clinical findings or roentgenograms demonstrate any appreciable amount of air or fluid within the pleural cavity, aspiration affords the most rapid and satisfactory therapy;<sup>17</sup> however, unless one is familiar with the usual roentgenologic signs following sympathectomy, one may be easily misled as to the presence or location of the pathologic changes in the bizarre roentgenograms which are not infrequently seen.<sup>17</sup> The value of early ambulation has urged us to employ it as early as is consistent with the patient's safety, but because of the hypotensive effects of sympathectomy it is necessary to use some caution, the patient always being accompanied until he has gained some strength and has become familiar with his new limitations.

*Neuralgia.*—Neuralgia is a familiar complication and may be exceedingly troublesome. Intercostal neuralgia is most frequent and may be minimized if care is exercised not to damage the nerve while freeing the rib, retracting the intercostal bundle, severing the rib anteriorly or, especially, disarticulating the rib at its costovertebral joint posteriorly. It has seemed to us that neuralgia has resulted even when no obvious damage had been done to the nerves, and for this reason we have attempted various measures in the hope of its prevention. Resection of the nerve has been done both alone and together with resection of the posterior root ganglion, but this does not prevent pain from adjoining intercostal nerves and may produce an unsightly bulging anesthetic area in the abdominal musculature. Injection of procaine hydrochloride or alcohol into the nerve root has been uniformly successful. Genitofemoral or ilioinguinal neuralgia is less common and less severe and is usually encountered after definite injury to the nerves while the lumbar sympathetic ganglions are being exposed or identified. The treatment of neuralgia in our hands has been, in general, unsatisfactory, and in cases such as case 4 there exists the necessity for careful handling to avoid the real danger of drug addiction. Fortunately, within two to three months the neuralgia has disappeared.

*Myalgia.*—Myalgia of the sacrospinalis or psoas muscle groups is usually the result of injury produced while attempting to obtain satisfactory exposure of the lumbar sympathetic chain. It has seemed to us that cutting the former muscle actually has added little to the exposure and has been responsible at times for the presence of postoperative

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17. Lord, J. W., Jr., and Hinton, J. W.: Operative and Postoperative Management of Hypertensive Patients Undergoing Thoracolumbar Sympathectomy. *New England J. Med.* **237**:840-843 (Dec. 4) 1947.

pain and weakness in the back. Injury to the psoas muscle is often the result of placement of the patient on the table which does not produce maximal relaxation of this muscle and thus demands the use of forcible and traumatic retraction. Management of the myalgia presents a problem similar to that mentioned in connection with neuralgia though fortunately the symptoms are usually somewhat less severe and less persistent.

*Hemorrhage.*—Hemorrhage from a major vessel has not been encountered in our series despite the proximity of the dissection to the large vessels. The vessels which we have found to be occasionally troublesome are the intercostal vessels when they are injured near the costovertebral junction high in the chest, the ascending lumbar veins and occasionally small phrenic vessels. Obviously, the problem is easily resolved by adequate exposure and by well controlled respirations combined with due caution. Generalized oozing from such an immense operative field is rarely a problem, but when present it may be a result of elevation of the blood pressure caused by straining, too rapid administration of fluids or, more often, accumulation of carbon dioxide. It has appeared that retropleural or incisional hematomas have been more frequent among our severely hypertensive patients. This might be in part explained by their elevated pressures, though we feel that the increased capillary fragility present in these patients may be a predisposing factor (case 5). For this reason we advocate the use of 50 mg of rutin four times a day as well as adequate doses of vitamin C pre-operatively and postoperatively, since others have demonstrated,<sup>18</sup> and we have found in our experience, that rutin will definitely reduce capillary fragility and will provide further protection against cerebral vascular accidents.

*Injury to the Thoracic Duct.*—Injury to the thoracic duct in the course of sympathectomy has not occurred in our experience, though conceivably this duct might be mistaken for the major splanchnic nerve and sectioned if proper identification were not made. Should this occur, it would appear that ligation of the cut ends of the duct would be the wisest course.<sup>19</sup>

#### REPORT OF CASES

CASE 1 (previously reported in the ARCHIVES<sup>12</sup>).—B. H., a 21 year old married woman, entered the Research and Educational Hospital on Nov. 2, 1939, complaining of severe continuous headache, nausea, vomiting and severe pain in the chest lasting for two weeks.

18. Griffith, J. Q., Jr., and Lindauer, M. A.: Increased Capillary Fragility in Hypertension, Incidence, Complications and Treatment, *Am. Heart J.* **28**: 758-762 (Dec.) 1944.

19. Berry, W. H.: Traumatic Chylothorax, *J. A. M. A.* **133**:319-320 (Feb. 1) 1947. Meade, R. M. J.: Case Report, Chicago Surgical Society, January 2, 1948.

She was well up to the age of 17, when, four months after being married, she had a miscarriage. Her physician told her that she would never have a full term baby. A few months later she again became pregnant; she was told of her high blood pressure and the albumin in her urine. Her feet were swollen. Labor was induced, and she was unconscious for two days. A year later she had continuous headaches and then again became pregnant. She lost this baby around the third month. After this, nausea and vomiting were frequent. In April 1939 paralysis of the right facial nerve occurred, and in September 1939 paralysis in the left facial nerve developed. Severe knifelike pain appeared under the left costal margin. She did not know whether her pressure fell or not during this time.

On her entrance to the hospital both eyegrounds showed papilledema, exudates and hemorrhages. Her blood pressure varied from 250 to 210 systolic and from 150 to 136 diastolic millimeters of mercury. Neither thiopental sodium (pentothal sodium®) given intravenously nor sodium nitrate or amobarbital sodium (amytal sodium®) administered orally was able to depress the diastolic pressure below 140 mm. Administration of potassium thiocyanate was ineffective. Renal function was greatly impaired, the urea clearance being depressed to 15 cc. per minute, but with no nitrogenous retention. The urine showed red blood cells and casts, with 0.2 to 1.4 Gm. of albumin daily. The heart was enlarged, and the electrocardiogram showed evidence of myocardial damage.

Operations on January 2 and 23, 1940, consisted of bilateral supradiaphragmatic section of the splanchnic nerves. At her discharge from the hospital the blood pressure had reached its preoperative level. She died at home, suddenly, two months later.

*Comment.*—Our results in patients with post-toxemic hypertension have been favorable when the original vascular injury has not repeated itself. The patient should have been sterilized after her first miscarriage, since in the course of the succeeding four years three pregnancies produced malignant nephrosclerosis which was unresponsive to both medical and surgical management and terminated fatally. We have operated on a few such patients at the urgent request of the internists, but our experience has been that no type of operation will materially influence the outcome. This stage should, therefore, be regarded as a contraindication to operation.

CASE 2.—A. T., a 46 year old white man, entered St. Luke's Hospital on April 14, 1947, complaining of hypertension of five years' duration which was discovered during a routine physical examination. Six months prior to his admission occipital headaches had developed but he had no other complaints.

On his entrance, examination revealed a blood pressure of 260 systolic and 155 diastolic. The heart was of normal size, the rate was 80 and the beat was of normal rhythm. The electrocardiogram showed the wave in lead I to be inverted and the T wave in lead II diphasic, and there was left axis deviation consistent with myocardial disease on the basis of damage to the coronary artery. Reactions to renal function tests were normal, there was no nitrogen retention and the intravenous pyelogram was normal. The basal metabolic rate was normal, but the Rumpel-Leede test showed twenty-five petechiae, and funduscopic examination showed advanced grade II angiospastic retinopathy. The blood pressure was still

labile, since by means of amobarbital sodium it could be reduced to 146 systolic and 100 diastolic.

*Operation.*—On April 23 sympathectomy from the ninth dorsal through the second lumbar ganglion, with resection of the splanchnic nerves, was done on the right side without production of pneumothorax, and a renal biopsy was performed, which showed group III renal hypertensive changes.

*Postoperative Course.*—On the day after the operation examination revealed atelectasis of the lower lobe of the right lung together with a small amount of fluid in the costophrenic angle, but this was rapidly corrected by carbon dioxide inhalations, which permitted the patient to cough up a large mucous plug, with subsequent complete aeration of the chest. The patient improved until five days later, when he became dyspneic, cyanotic and cold, and moist rales could be heard throughout the entire chest. The pulse rate rose to 125, and a gallop rhythm appeared. Clinically the patient exhibited pulmonary edema and left ventricular failure. An electrocardiogram taken at this time showed the T waves in leads I and II inverted and the T wave in lead III depressed as well as depression of the S-T segment in leads II and III, which was diagnosed as consistent with myocardial disease only. The patient was given oxygen, compression bandages were placed about the legs and he was given aminophylline. On the following day he was also given 2 cc. of a mercurial diuretic, and in the subsequent twenty-four hours he excreted 3,940 cc. of urine. During the next four days the blood pressure became elevated from 90 systolic and 70 diastolic to 180 systolic and 100 diastolic, the pulse rate fell to 88 and a normal rhythm was established. The clinical signs of heart strain and pulmonary edema disappeared, and repeated electrocardiograms were similar to those taken on the patient's admission. He gradually improved so that by the twenty-third postoperative day he was able to walk several hundred yards without dyspnea. His electrocardiogram showed no further changes, and a roentgenogram of the chest showed only evidence of resorption of a small amount of blood or fluid from the right retropleural space. The patient was discharged to his home to recuperate before the second stage of the operation was attempted.

On June 22 the patient was readmitted. At this time his blood pressure was 230 systolic and 140 diastolic, his pulse rate was 80 and regular and the chest was normal clinically although roentgenograms still demonstrated a slight area of increased density just above the right side of the diaphragm. The blood was normal on chemical examination, and an electrocardiogram showed only those changes demonstrated during the original hypertensive study.

*Operation.*—On May 27 sympathectomy from the ninth dorsal through the second lumbar ganglion, with splanchnic resection, was done on the left side without the production of pneumothorax, and the patient left the operating room in good condition.

*Postoperative Course.*—The day after operation the patient had a blood pressure of 108 systolic and 70 diastolic, the pulse was regular, the respiratory rate was 24 and the chest was clear. He did, however, have definite facial paralysis on the left side. It is of interest in this connection that after operation on a mastoid at the age of 7 the patient noted facial paralysis, but this had improved to the extent that it had not been noted on preceding examinations. The following day his pulse rate mounted to 150, the respiratory rate increased to 36 and the patient became dyspneic. He also suffered from profuse diaphoresis of the nondenervated portions of the body. Clinical and roentgenologic examination of the chest at this time

showed no abnormalities. The blood pressure was still 110 systolic and 80 diastolic, but the radial pulse had become imperceptible though an electrocardiogram showed no change. Later spastic paraplegia developed on the right side, the head and eyes deviated toward the right and for a short period there was a loss of consciousness. The pallor of the patient suggested a profound alteration in the circulating blood volume as being responsible for the neurologic symptoms rather than a cerebral vascular accident. Treatment consisted in the administration of 0.3 cc. of phenylephrine hydrochloride (neosynephrine hydrochloride®) intravenously, 7½ grains (0.5 Gm.) of aminophylline intramuscularly every six hours, 3 cc. of adrenal cortical extract intramuscularly every six hours, 1½ grains (0.1 Gm.) of digifolin® (a digitalis preparation) twice daily, 500 cc. of blood and oxygen by mask. The blood pressure under this treatment gradually improved over the succeeding ten days, and all signs of paralysis rapidly disappeared. The patient did, however, acquire a severe and persistent hiccup which failed to respond to the ordinary forms of treatment and which after some sixty hours was finally controlled only by blocking the phrenic nerve with procaine hydrochloride. By July 10 the patient had sufficiently recovered to sit in a wheelchair for short periods, but postural hypotension and concomitant elevation of the pulse rate were so excessive that he was not permitted to be ambulatory until several days later. At the time of his discharge on July 24 the horizontal pressure was 120 systolic and 80 diastolic, the electrocardiogram was no different from that made on his original examination and roentgenograms showed only the changes usually associated with sympathectomy. Reexamination five months later revealed a horizontal blood pressure of 130 systolic and 80 diastolic, and no dyspnea on exertion. The patient was able to perform eight hours' work in a factory. Two and a half years later his status was the same.

*Comment.*—This case serves as an example of several of the dangers encountered in operations for hypertension. After an uneventful operation, atelectasis developed in a patient with advanced grade II hypertension, which fortunately responded satisfactorily to therapy. A further complication, the presence of a small amount of retropleural bleeding which was not massive enough to require aspiration and which did not materially influence the patient's course, was also noted. However, after each surgical procedure he showed evidence of general circulatory collapse which was attributable to alteration of the blood volume, decreased venous return and myocardial insufficiency. Pulmonary edema, peripheral circulatory failure and the presence of a shocklike state were evidence of this fact, as was the favorable response to measures designed to support blood volume and increase cardiac compensation. After the second operation this patient showed not only signs of cardiac failure but evidence of profound cerebral anoxia, as was well demonstrated by accentuation of previously undetected latent cerebral damage, unconsciousness and the appearance of spastic paraplegia. Heroic measures alone were able to save him after a stage operation for hypertension, and we were convinced that he would have failed to survive a one stage procedure. Despite his stormy convalescence, it

would appear that he has suffered no permanent cerebral damage from his experience, and clinically he has obtained a good result from the sympathetic denervation. The aid of the medical service in such cases is invaluable.

**CASE 3.**—E. G., a 52 year old Negro woman, entered St. Luke's Hospital on March 13, 1947, complaining of mild headaches, dizzy spells and some substernal pain which was precipitated by exertion or by emotional excitement. She gave no history of dyspnea or of episodes of cardiac decompensation.

On her entrance to the hospital, the patient's blood pressure was 230 systolic and 140 diastolic. Her heart was of normal size, though an electrocardiogram showed evidence of recovery from an old anterior coronary occlusion. After evaluation, her condition was diagnosed as early grade III hypertension, but since her pressure was still somewhat labile it was thought that she might benefit from surgical intervention.

**Operation.**—On March 22 sympathectomy from the ninth dorsal through the second lumbar ganglion was done on the right side, together with resection of the splanchnic nerve, without the production of pneumothorax. The patient left the operating room in good condition.

**Postoperative Course.**—Postoperatively the blood pressure was 110 systolic and 70 diastolic, the pulse rate was 100 and regular and the respiratory rate was 16. The morning after operation the temperature was 101 F., the pulse rate was 68 and the respiratory rate was 32. A slight cough had also developed, and there were rales present in the bases of both lungs. The evening of this same day the patient suddenly became cold and clammy, the pulse became rapid and despite supportive therapy she died.

**Pathologic Examination.**—This showed the presence of a recent thrombosis on the right coronary artery, with early infarction of the myocardium of the left ventricle and ventricular septum. The lungs showed moderate hyperemia and edema. The remainder of the changes were typical of relatively advanced hypertensive disease.

**Comment.**—It is, of course, open to speculation whether the operative load, a postoperative decrease in the rate of coronary blood flow combined with increased coagulability of the blood in the postoperative state or coincidence should bear the responsibility for this fatality. In any event the hazards of surgical intervention in patients with severe hypertension were clearly demonstrated.

**CASE 4.**—M. D., a 42 year old white woman, entered St. Francis' Hospital, Evanston, Ill., on Jan. 22, 1947, complaining of hypertension of three years' duration, recurrent attacks of headache, dizziness, tinnitus, epistaxis and occasional attacks of dyspnea, orthopnea and palpitation.

The past history revealed three previous normal pregnancies followed by a fourth pregnancy which had terminated in spontaneous abortion during the fifth month. The patient's blood pressure, however, was said to have been normal immediately after this abortion. She had had numerous surgical procedures performed, among which may be enumerated appendectomy, removal of the tubes and one ovary, cholecystectomy and gastroenterostomy.



On her entrance to the hospital the blood pressure was 170 systolic and 120 diastolic. Fundusoscopic examination revealed grade II retinopathy. The basal metabolic rate, the electrocardiogram and the roentgenogram of the chest were normal; chemical studies of the blood and renal function tests gave normal results. With administration of amobarbital sodium, the blood pressure fell to 110 systolic and 70 diastolic. Surgical intervention was recommended for grade II hypertension.

*Operation.*—On Feb. 6, 1947, sympathectomy from the eighth dorsal through the third lumbar ganglion, with resection of the splanchnic nerve, was done, and a renal biopsy was performed, which showed grade II hypertensive changes.

*Postoperative Course.*—The postoperative course was uneventful except for the presence of patchy atelectasis and mild pain in the area of the right loin until the sixth day, when pain in this area became so severe as to prevent sleep. For the succeeding three weeks the patient complained almost constantly of pain, which was only partially relieved temporarily by the use of acetylsalicylic acid, meperidine hydrochloride, pantopon® (a mixture of hydrochlorides of the opium alkaloids) alone or in combination with barbiturates, bromides or chloral hydrate. Several blocks of the right genitofemoral nerve and the intercostal nerves with procaine hydrochloride produced only temporary relief, while hot water bottles or local diathermy followed by massage and small doses of roentgen rays to the loin area produced no improvement. Hot sitz baths and support to the patient's back directly and by means of a fracture board beneath the mattress did provide some relief, although pain was present in some measure even at the time of her second operation.

*Operation.*—On Feb. 25, 1947, sympathectomy from the eighth dorsal through the third lumbar ganglion, together with splanchnic resection, was performed on the left side uneventfully.

*Postoperative Course.*—The postoperative course was uneventful except for the appearance of intercostal neuritis on the left side, which overshadowed the residual neuritic complaints remaining from the first operation. The various forms of therapy previously mentioned were again employed, but they provided only limited control of the pain. The patient left the hospital on March 4, with a blood pressure of 120 systolic and 80 diastolic, still suffering from some neuritic pain. She was followed at home by her family physician, who felt it necessary to employ codeine and acetylsalicylic acid for control of her pain and the routine use of barbiturates at night for a period of several months, until the question of drug addiction became a real one. It was only with difficulty that all medication was withdrawn.

It is interesting to note that menstruation, which had occurred only once in the preceding eighteen months in this patient, recommenced after her second operation, appearing at regular intervals and persisting for several months thereafter in the absence of any demonstrable pelvic disease.

*Comment.*—A patient who has undergone such a number and variety of operations is always seen with a somewhat skeptical eye by a consulting physician. However, the evidence of hypertensive vascular disease which had failed to respond to medical management and which appeared to be amenable to surgical measures urged the use of the latter. The possibility of reactivation of the ulcer for which the

previous gastroenterostomy had been performed has been kept in mind, but as yet this complication has not arisen. This type of case poses the difficult problem of determining the presence and severity of the pain of which the patient complains so bitterly. If time and the diagnostic use of placebos confirm the patient's story, the treatment of intractable neuralgia must be faced. Therapy, it must be admitted, is largely a matter of psychologic support combined with therapeutic trial and error until time brings relief. A desire to relieve the patient's pain must be wisely tempered by a healthy respect for the knowledge of the ease with which drug addiction can be produced in persistent cases. The relationship of menstruation to sympathectomy in this case may be coincidental, though removal of the sympathetic tonus to the vessels supplying the ovaries or uterus might occasionally produce a sufficiently improved blood supply, so that increased or more regular menstrual flow might result.

**CASE 5.**—V. B., a 32 year old white woman, entered St. Luke's Hospital on Feb. 3, 1947, complaining of high blood pressure of fifteen years' duration, occipital and frontal headaches, dizziness, spots in front of her eyes, fatigue, palpitation and some pain in the chest and dyspnea on moderate exertion.

**Past History.**—In 1941 this patient had undergone a subdiaphragmatic splanchnic resection elsewhere because of hypertension. After this she was confined to bed for almost two years and was unable to perform her housework because of weakness and chronic fatigue. She had also been troubled by severe sweating of the nondenervated portions of the body.

**Examination.**—On her entrance to the hospital examination revealed a slightly undernourished, nervous woman who appeared to be fairly well except for a blood pressure of 240 systolic and 120 diastolic. Although the roentgenograms of her chest and the pyelograms showed no abnormality and renal function was satisfactory, the electrocardiogram showed changes compatible with hypertensive cardiovascular disease. Examination of the fundi showed grade III arteriosclerotic retinopathy and the Rumpel-Leede test showed about 280 petechiae within a 1½ inch (3.8 cm.) radius. The patient was considered to have grade III hypertension, but it was felt that she might still receive some benefit from further sympathetic denervation.

**Operation.**—On February 15 sympathectomy from the eighth dorsal through the second lumbar ganglion, with removal of the supradiaphragmatic portion of the splanchnic nerve, was done on the left side and a renal biopsy was taken which showed focal scarring and nephrosclerosis of the kidney of an advanced type.

**Course.**—The patient returned from the operation in good condition, and the chest appeared to be well aerated. However, on the following day she complained of some incisional pain and had a temperature of 102.4 F.; the respiratory rate was increased, and some dulness was noted in the left side of the chest. After elevation of a mucous plug from the lung and with the help of penicillin therapy, all respiratory symptoms cleared up rapidly. For the first few days abdominal distention was noted, though there was no nausea or vomiting and the patient was passing gas rectally. She appeared to be apathetic and fatigued but had no significant complaints until the seventh postoperative day, when she

complained of pain in her incision. Some fluctuation was noted in the wound; aspiration yielded 30 cc. of bloody fluid, and smaller amounts were withdrawn on two subsequent occasions. A roentgenogram of the chest which was taken at this time showed no evidence of intrapleural disease. Three weeks later a roentgenologic examination of the chest showed an increased density in the left region extending up to the fourth rib anteriorly and obliterating the left border of the heart and diaphragm. The heart was displaced toward the right, and left hilar shadows were increased. Within the next three days 2,000 cc. of bloody serum was aspirated from the thoracic cavity. The patient was discharged on March 22 to complete her recovery before the second stage of her operation was performed. The second stage was later carried out, with an equally stormy convalescence.

*Comment.*—This case illustrates the severe incapacitation which may accompany even minimal sympathetic denervation in advanced cases. The severity of the patient's hypertensive status was paralleled by the marked evidence of increased capillary fragility. Though capillary fragility may have been favorably influenced by the preoperative use of rutin and vitamin C, a bleeding tendency may have been responsible for the complications seen during the convalescent period: abdominal distention, which may have resulted from retroperitoneal bleeding, formation of hematoma in the wound and possibly considerable intrapleural or retropleural accumulation of serosanguineous fluid. The increased incidence of these complications in other hypertensive patients suggests such causal relationship. The excessive and persistent hyperhydrosis of which the patient complained on her admission to the hospital represented the compensatory result of increased sympathetic tonus in the nondenervated portions of the body, and this was accentuated after completion of the surgical treatment, so that even mild Raynaud's phenomenon was at times noted in the upper extremity.

#### SUMMARY

The undesirable side effects of sympathectomy for hypertension are due to postural hypotension, compensatory accentuation of vasomotor tonus of the nondenervated portions of the body and alterations of sensory and motor innervation of the visceral organs. These may be expected to some degree in all cases.

The selection of cases of hypertension suitable for denervation is still so poorly understood that prediction of operative results in all cases is impossible. The contraindications to surgical treatment of hypertension depend basically on the degree of cerebral, cardiac and renal damage already sustained by the patient as well as on the condition of the peripheral vessels as demonstrated by the lability of the blood pressure to vasomotor tests.

Organic and physiologic changes in the cardiovascular, renal and cerebral systems will result in complications in a definite percentage

of patients subjected to sympathectomy for hypertension. Proper selection of cases will diminish the anticipated incidence, though in our experience this has amounted to 7 per cent. Severe, prolonged and intractable myalgia and neuralgia occurred postoperatively in 13 per cent of our cases despite extreme care and were the major cause of complaint on the part of the patients. Hydrothorax, hemothorax, pneumothorax and atelectasis were encountered in 23 per cent of our cases but were rarely a problem.

The postoperative morbidity rate of sympathectomy for hypertension was below 10 per cent and the mortality rate below 1 per cent.

Sympathectomy is of definite benefit in the treatment of hypertension, but the benefits must be weighed carefully against the inherent disadvantages, possible complications and at times uncertain results which will be encountered in any large group of even carefully selected cases.

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## LUMBAR SYMPATHECTOMY FOR ARTERIO-SCLEROTIC GANGRENE

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THE VALUE of sympathetic block with procaine hydrochloride and of lumbar ganglionectomy in the treatment of acute arterial occlusion due to accidental arterial laceration, embolism, thrombophlebitis and its sequelae, Raynaud's disease, hyperhidrosis and certain instances of Buerger's disease is now well established. The use of sympathectomy for arterial deficiency due to arteriosclerosis, however, has not been generally accepted because of the extensive and irreversible changes which occur in the arteries in this disease and the frequency of failure of this type of treatment in poorly selected cases.

In 1931 Flothow<sup>1</sup> reported 8 cases of arteriosclerosis of peripheral vessels in which improvement was obtained by injection of alcohol into lumbar sympathetic ganglions. Two of the patients had actual gangrene of one or more toes. In 1 of these the pain was relieved and the temperature of the skin raised 10 C. (18 F.). Although amputation was necessary at a later date "because of a functionally useless left leg," the disease appeared to be temporarily arrested by this procedure. In the second of the 2 cases of gangrene of the left great toe, the necrotic area "eventually cleared up" after injection of alcohol into the lumbar sympathetic ganglions. A diagnostic sympathetic block, with determinations of the cutaneous temperature, preceded the alcohol injections in each case. A troublesome alcohol neuritis occurred in most instances, lasting from two to six weeks.

In 1932 Robertson<sup>2</sup> reported the use of sympathectomy in a number of cases of impending gangrene from arteriosclerosis and intermittent claudication with numbness and pain in the extremities. When the

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1. Flothow, F. G.: Sympathetic Alcohol Injection for Relief of Arteriosclerotic Pain and Gangrene, *Northwest Med.* **30**:408-412 (Sept.) 1931.

2. Robertson, D. E.: Treatment of Vascular Diseases of the Extremities by Sympathectomy, *J. Bone & Joint Surg.* **14**:57-65 (Jan.) 1932.

arteriosclerosis was complicated by diabetes, pain was diminished by sympathectomy but ulcerations were not healed. Pain was relieved and more conservative amputations were possible when insulin therapy and sympathectomy were combined.

In 1937 Baker<sup>3</sup> reported the use of paravertebral injection of 95 per cent alcohol in a patient with arteriosclerotic gangrene of the distal half of the foot whose opposite leg had previously been amputated at mid thigh for the same cause. Amputation of the other leg at mid-thigh level later became necessary, but the gangrenous process was temporarily retarded by the alcohol injection. Harris<sup>4</sup> in 1941 reported the results of lumbar sympathectomy in 13 cases of arteriosclerotic peripheral vascular disease. The temperature of the skin was determined after paravertebral block in each case. If a rise of 3 C. (5.4 F.) in the temperature of the skin could be obtained after block, Harris felt that a good result could be anticipated after sympathectomy. Sympathectomy was performed in most cases of severe peripheral arteriosclerosis, but it was his opinion that the operation should be carried out before ulceration or gangrene made its appearance, as these processes so greatly increase the demand for circulation. Among the 13 cases reported there were five good results, one fair result and seven poor results. In some patients showing little or no rise in the temperature of the skin after spinal anesthesia good results followed lumbar sympathectomy.

In 1941 Atlas<sup>5</sup> pointed out that conservative dilation therapy would not relieve peripheral ischemia unless the peripheral resistance to blood flow in the small vessel bed of the ischemic part was decreased by interruption of its sympathetic innervation. He also pointed out the danger of sympathectomy in advanced cases characterized by marked pallor of the foot on elevation or rubor on dependency, dry inelastic skin, venous filling of more than fifteen seconds and severe subjective and objective coldness of the foot without a rise in the temperature of the skin to 28 C. (82.4 F.) after sympathetic block. In such cases the collateral vascular network is incapable of hypertrophy and the small vessel bed is inflexible. The gangrenous process, if present, may rapidly increase after sympathectomy. Atlas reported 20 lumbar sympathectomies (performed by simple division of the trunk and burying of the lower end). There was immediate relief of severe persistent

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3. Baker, W.: Alcohol Injection of Lumbar Sympathetic Ganglia in Arteriosclerosis of the Extremities, *M. Ann. District of Columbia* 6:9-14 (Jan.) 1937.

4. Harris, R. I.: Obliterative Vascular Disease: Treatment by Sympathectomy, *Canad. M. A. J.* 45:529-533 (Dec.) 1941.

5. Atlas, L. N.: Lumbar Sympathectomy in Treatment of Selected Cases of Peripheral Arteriosclerotic Disease, *Am. Heart J.* 22:75-85 (July) 1941.

coldness, numbness and paresthesia and improvement in ulceration. Elevation of cutaneous temperatures of from 6.5 to 11.5 C. (11.7 to 20.7 F.) was obtained and improvement in oscillometric pulsations and intermittent claudication after a period of from six months to a year (when collateral circulation had developed).

Telford and Simmons<sup>6</sup> described the results of sympathectomy in 98 patients with peripheral arteriosclerosis at the Neurovascular Clinic of the Manchester Royal Infirmary during the past fifteen years. There were 4 deaths (1 due to alcoholism, 1 to duodenal ulcer and 2 to pulmonary embolism). Eighty-eight cases were followed closely. In 47 of these, in which sympathectomy was performed for intermittent claudication, there was some improvement in symptoms in all instances. Forty-one sympathectomies were performed for gangrene or incipient gangrene. In 21 cases there were good results (separation and healing of minor ulcerations enabling a life of reasonable activity after previous invalidism). In 20 cases the operation did not succeed and some form of amputation was later necessary. These amputations were often of a limited extent, however. Their results showed that if gangrene is more than trivial, sympathectomy should not be performed, especially if it is complicated by infection. In 2 cases there was distinct extension of the gangrenous process after operation.

De Takats, Fowler, Jordan and Risley<sup>7</sup> pointed out the inadvisability of sympathectomy in instances in which there is no increase in the temperature of the skin or rather a paradoxical fall following paravertebral block, as in such instances sympathectomy precipitates gangrene. When there is a rise in the temperature of the skin following paravertebral block as well as improvement in walking ability and shortening of the venous filling time, sympathectomy was deemed advisable. They divided patients in four classes, as follows:

1. Middle-aged persons with a walking ability of a few blocks and absence of popliteal or femoral pulsations. Good results were obtained after lumbar sympathectomy in 9 such patients.

2. Middle-aged or elderly persons with a walking ability of from one-half to two blocks showing some vascular stasis. Operations were performed on 10 such patients to prevent gangrene. Although there was no improvement in walking ability after operation, gangrene did not develop in any of these patients.

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6. Telford, E. D., and Simmons, H. T.: Sympathectomy in Peripheral Arteriosclerosis, *Brit. M. J.* **1**:386-387 (March 16) 1946.

7. de Takats, G.; Fowler, E. F.; Jordan, P., and Risley, T. C.: Sympathectomy in Treatment of Peripheral Vascular Sclerosis, *J. A. M. A.* **131**:495-499 (June 8) 1946.

3. Patients requiring amputation who had already had one leg amputated. Preliminary lumbar sympathectomy permitted amputation of the toes in 3 such patients and amputation of the lower part of the leg in 3, in instances formerly requiring supracondylar amputations.

4. Persons with intractable pain, diffuse osteoporosis and glossy edema typical of the causalgic state in whom the peripheral nerves were demyelinated in patches were operated on. Five such patients were improved after lumbar sympathectomy; none required amputations.

These investigators noted four results following sympathectomy in cases of arteriosclerosis: 1. The extremity warmed faster and cooled more slowly on direct exposure. 2. A high vasoconstrictor tonus in a standing or sitting position was abolished. 3. Vascular exercises and intermittent vascular hyperemia were more effective. 4. Any cross stimulation between sympathetic and demyelinated sensory fibers was abolished.

#### CLINICAL MATERIAL AND TECHNIC

Nineteen patients suffering from late peripheral arteriosclerosis with necrotic phenomena were subjected to lumbar sympathectomy. They ranged in age from 51 to 84 years. Fifteen patients were Negroes, 5 of them women, 2 were white women and 2 were white men. The significance of these comparative figures of race and sex is greatly distorted by the fact that the ratio of the population of the Gallinger Municipal Hospital was approximately 3.2 Negroes to 1 white person for this period. Nine of the patients suffered from diabetes mellitus.

The elected type of operative procedure consisted of a muscle-splitting transverse incision at the level of the twelfth rib and the umbilicus. The external oblique muscle is split in the direction of its fibers, and the internal oblique and transversalis fibers are separated at one time. The blunt dissection of the peritoneum away from the surgical area is facilitated by the lateral positioning of the patient, which introduces the effect of gravity on the peritoneum and its contents. The second and third lumbar ganglions are enucleated; the fourth ganglion, which was removed in the early cases, is now left intact.

#### LUMBAR SYMPATHECTOMY FOR ARTERIOSCLEROSIS WITH NECROSIS

##### PRESENTATION OF CASES

CASE 1.—I. K., a 65 year old white man, was admitted to the hospital on Feb. 17, 1947, with the diagnosis of diabetes and early arteriosclerotic gangrene of the left fourth and fifth toes. The right leg had been previously amputated at the mid thigh. Pulsations of the popliteal, dorsalis pedis and posterior tibial arteries were absent. Sympathetic block of the second, third and fourth lumbar ganglions produced increase in temperature, with relief of pain. A lumbar sympathectomy



involving the second and third ganglions was performed on the left side on March 18, 1947. Discoloration of the affected toes disappeared. Follow-up examinations from the time of the operation until Jan. 20, 1948 revealed that the right foot exhibited the original response to sympathectomy. The foot remained warm, well healed and free of pain until January 23, when he was readmitted for mild cellulitis of the second right toe. The inflammation disappeared after three days of rest in bed.

CASE 2.—F. W., a 63 year old Negro, was admitted on Dec. 27, 1946, with the diagnosis of old cerebrovascular accident, general arteriosclerosis and a large superficial gangrenous area on the anterior surface of the left knee and the upper part of the leg. A roentgenogram showed no pathologic changes in the bone; arteriosclerosis of the femoral and tibial vessels was noted. Pulsations of the dorsalis pedis, posterior tibial and popliteal arteries were absent. The lesion gradually sloughed and extended in spite of adequate débridement and local treatment. On Jan. 23, 1947, a lumbar sympathectomy was performed on the left side. The extension of the ulceration ceased, and healing began. On March 4, a split thickness skin graft was applied successfully. The patient was discharged on May 1, completely healed. The last follow-up examination, on Feb. 5, 1948, revealed the area to be completely healed. The left extremity was warmer than the right, though the pulsation remained absent as originally.

*Comment.*—This is an example of a bizarre type of gangrene which was progressing until sympathectomy was performed. The operation was of definite value in permitting reparative grafting.

CASE 3.—M. S. O., a 78 year old Negro woman, was admitted to the hospital on April 6, 1947, with discoloration of the left first toe and the foot associated with roentgenologic evidence of arteriosclerosis of the aortic and leg vessels. There were no palpable pulsations of the arterial trunks below the knee. The left foot was cool and constantly painful. Lumbar sympathetic block caused decrease in pain and increase in temperature of the skin. On April 30, 1947, lumbar sympathectomy was performed on the left side. The discoloration and pain gradually disappeared. The patient was discharged from the hospital on May 9, 1947.

CASE 4.—D. D., a 51 year old Negro woman, was admitted to the hospital with the diagnosis of diabetes and arteriosclerotic gangrene of the distal half of the left foot. There was no pulsation of the dorsalis pedis artery, and pain was sharp and intermittent in character. Lumbar sympathetic block relieved the pain and increased the temperature of the skin slightly. The gangrene continued to extend. On Feb. 13, 1947, lumbar sympathectomy was performed on the left side. The gangrene continued to extend until it involved the lower half of the leg, when a supracondylar amputation was done. The stump healed without pain and remained warmer than the opposite thigh.

*Comment.*—This case represents a complete failure of ganglionectomy to interrupt or modify the extension of gangrene.

CASE 5.—C. F., a 53 year old Negro with diabetes, was admitted on March 21, 1947. A midthigh amputation of the right lower extremity had been carried out previously. The left foot showed ulceration and gangrenous discoloration of the middle toe. Poor pulsations were felt in the dorsalis pedis and posterior tibial vessels. With sympathetic block the temperature of the skin increased, and the amplitude of the pulsations was slightly increased by oscillometric measurement. Lumbar sympathectomy performed on the left side on April 4 gave a good

response. The toe was amputated at the time of the operation; the stump healed well. One month later the patient succumbed after an elective surgical procedure. The left lower extremity remained markedly improved during this time.

*Comment.*—Only the immediate effect could be noted in this case, which was prompt and definite.

CASE 6.—M. W., a 73 year old Negro woman, was admitted on June 27, 1947. Supracondylar amputation had been performed previously on the left side. The right foot was at first discolored about the heel, but then it became gangrenous and painful in this area. A sympathetic block produced a positive effect. On August 29 sympathectomy was performed on the right side. The discoloration disappeared, and the ulceration gradually healed completely. A follow-up check on Jan. 20, 1948, revealed that the foot had remained well healed; the effect of sympathectomy was evident. The psychologic effect was excellent since the patient was able to move about easily on crutches without pain.

*Comment.*—Sympathectomy seemed to interrupt the process and facilitate excellent healing in this instance.

CASE 7.—A. S., a 63 year old Negro man, was admitted on July 30, 1947, with the diagnosis of early gangrene of the great toe of the left foot due to arteriosclerosis. No pulsation was felt in any vessel below the femoral. The fundi showed arteriosclerotic changes. Several lumbar blocks had a positive effect. Lumbar sympathectomy performed on the left side on August 11 produced warming, relief of pain and disappearance of the discoloration of the great toe. Attempts at follow-up were unsuccessful.

*Comment.*—This case represents an excellent immediate response. It is unfortunate that later observations were not possible.

CASE 8.—E. F., a 53 year old diabetic Negro woman, was admitted on July 6, 1946, with arteriosclerotic ulceration at the base of the third and fourth toes. While she was in the hospital the ulceration progressed to include the second, third, fourth and fifth toes and the distal half of the lateral two thirds of the foot. The gangrene was so extensive that several members of our attending staff advised supracondylar amputation, but the patient consistently refused to submit to this. Amputation of the toes was consented to and was carried out on August 12. Because of poor healing of the stump, a lumbar sympathectomy was performed. The stumps healed rapidly after the operation.

*Comment.*—This case indicated that radical amputation is not necessary in many cases of extensive necrosis of the foot. Healing is implemented by sympathectomy.

CASE 9.—B. S., a 69 year old Negro woman, was admitted on March 6, 1947, with the diagnosis of diabetes and arteriosclerotic gangrene of the right second toe. The right third toe had been amputated for gangrene three years previously. No pulsations of the dorsalis pedis or posterior tibial arteries were present. The condition of the toe improved after rest in bed to the point where amputation was not considered necessary. Lumbar sympathetic block produced slight increase in the temperature of the skin. Lumbar sympathectomy was performed. Follow-up examinations, the last of which was made on Jan. 20, 1948, showed that the healing remained good, with a full response to sympathectomy.

*Comment.*—This case demonstrates that healing of the stump after amputation of the toe in instances of arteriosclerotic gangrene for at least three years is possible without sympathetic denervation. Also, it shows the difficulty of proper evaluation of the results of lumbar ganglionectomy in arteriosclerosis.

CASE 10.—I. S., a 76 year old Negro woman, was admitted on Sept. 26, 1946, with arteriosclerotic gangrene of the fourth and fifth toes of the right foot. Lumbar sympathetic block with procaine hydrochloride was carried out on October 22, with an immediate increase in the temperature of the skin. The dorsalis pedis and posterior tibial pulsations were absent. Lumbar sympathectomy was done on the right side on October 28. The toes were amputated subsequently, and the stumps healed well. Follow-up studies indicated that the response continued, with no change in the healing. The last check-up on Jan. 20, 1947, showed the affected foot well healed. The patient walked about without pain. The foot and leg were much warmer than the unaffected side.

*Comment.*—This result is good as far as healing is concerned and particularly in regard to duration of the sympathetic response.

CASE 11.—L. C., a 62 year old white woman, was admitted on July 16, 1947, with a seventeen year history of diabetes mellitus. An arteriosclerotic ulcer which had begun on the plantar surface of the right first toe six months before her admission had never healed and now consisted of a deep crater. The left great toe had been removed before at another hospital. The area around the crater became reddened, swollen and localized, and a large amount of thick yellow-white pus was finally evacuated. Roentgenograms showed evidences of osteomyelitis in the bones of the big toe. Pulsation of the dorsalis pedis was decreased but present. Though sympathetic block failed to increase the temperature, sympathectomy was carried out on August 7. It resulted in considerable warming of the right foot, with disappearance of pain. The ulcer and the incisions healed readily. A final check-up on Jan. 7, 1948, demonstrated the right foot to be well healed, free of pain and still much warmer than the left.

*Comment.*—This case shows the effect of sympathetic interruption on early necrosis and infection associated with arteriosclerosis. It may be noted that the patient recovered readily after amputation of another toe four years before, without ganglionectomy.

CASE 12.—J. H., a 67 year old Negro, was admitted on Jan. 8, 1945, with the diagnosis of arteriosclerotic ulcer of the right great toe. Pain was cramp-like in character, being present during the night. The dorsalis pedis and posterior tibial arterial pulsations were not palpable. Lumbar sympathectomy was performed on the right side on February 1. This eliminated the pain in the toe, but did not prevent a gas gangrene infection of the amputated toe stump, which necessitated a supracondylar amputation. The second and third lumbar ganglions on the left were also removed during the patient's stay in the hospital. A final check-up on Feb. 16, 1948, revealed the amputation stump to be well healed and free of pain. The left leg showed no abnormalities and was warm.

*Comment.*—This represents a failure of the operation to effectuate adequate healing of the amputated toe. Again it is interesting to note the duration of the effect of ganglionectomy.

CASE 13.—H. H., an 84 year old Negro woman, was admitted on July 16, 1947, with gangrene of the fourth and fifth toes and controlled diabetes mellitus. She had complained for several months of severe lancinating pain at night and during poor weather. No dorsalis pedis or posterior tibial pulsations were present. On August 8 lumbar sympathectomy on the right side and amputation of the right third, fourth and fifth toes were done. This resulted in marked relief of pain and progressive though slow healing of the amputation stumps. A

final check-up on Feb. 17, 1948 found the patient free of pain and walking about with the help of a cane. The stumps had remained well healed, and the effect of sympathetic denervation was still definite.

*Comment.*—In view of the age of the patient and the severity of the organic process, this is to be considered a noteworthy result.

CASE 14.—A. A., a 70 year old white man, was admitted on Dec. 5, 1947, with gangrene of the right second, third, fourth and fifth toes which had become apparent ten days previously. Sympathetic block gave a good response. No dorsalis pedis or posterior tibial pulsations were present. The gangrene spread to include all of the foot. Lumbar sympathectomy was finally performed on the right side on December 22, together with amputation below the knee. The stump healed well, and the leg remained warm and of larger size than the unaffected leg.

*Comment.*—Sympathectomy probably was important in preserving the knee joint for a successful amputation below the knee.

CASE 15.—M. J., a 57 year old Negro woman with severe diabetes, was admitted on May 10, 1947, with early gangrene of the left foot. Sympathetic block and sympathectomy were completely unsuccessful in limiting the necrotic process. Consequently, a supracondylar amputation was carried out. The stump healed well. A final check-up on Feb. 5, 1948, revealed the stump to be well healed.

*Comment.*—This case is an example of failure of the operation to affect the necrotic process.

CASE 16.—P. P., a 71 year old Negro man, was admitted with an arteriosclerotic gangrenous ulcer at the base of the great toe. Sympathetic block produced striking relief of pain and slight increase in the temperature of the skin. Lumbar sympathectomy performed on the right side on June 2, 1947, produced a good immediate result consisting of pronounced decrease in pain, healing of the ulcer and good increase in the temperature of the skin. However, he was readmitted on July 17 with a recurrence of the ulcer. The gangrene progressed despite all measures, and a supracondylar amputation was resorted to. The stump healed well.

*Comment.*—This case must be considered as a failure. Because of the time interval it is doubtful that the operation precipitated the gangrene, but the relationship may be questioned.

CASE 17.—D. S., a 70 year old Negro woman, was admitted with a history of severe nocturnal pain in the right foot and gangrene of the right fourth toe. The right foot was much cooler than the left; dorsalis pedis and posterior tibial pulsations were absent. Sympathetic block gave a good response. Sympathectomy and amputation of the toe were carried out on Feb. 12, 1948. The immediate effects were good in terms of cessation of pain and beginning of healing.

CASE 18.—S. W., a Negro woman aged 62, was admitted on Sept. 28, 1946, with a history of diabetes, extensive generalized arteriosclerosis and the presence of gangrene involving the fourth and fifth toes and circumscribing the foot. Lumbar blocks gave a good response. Penicillin and local treatment showed no effect. Lumbar sympathectomy, which was performed on November 19 produced healing of the area after amputation of the fifth toe and skin grafting of part of the defect. Osteomyelitic changes in the bone, which were demonstrated on the preoperative roentgenograms, regressed also. A final check-up on Jan. 20, 1948, showed the healing to be complete. The patient was free of pain and walked about easily without support.

CASE 19.—E. S., a 62 year old diabetic white woman, was admitted on May 13, 1947, with symptoms of intermittent claudication of both feet and ulceration of the dorsum of the right foot. There was an excellent response to sympathetic block bilaterally. Bilateral sympathectomy was carried out. The result was excellent; a marked decrease in the degree of claudication, healing of the ulcer and continuous increase in the temperature of the skin were demonstrated. A check-up on Feb. 5, 1948 showed no change in the excellent response.

### SUMMARY

Nineteen patients suffering from peripheral arteriosclerosis with evidence of tissue necrosis were subjected to lumbar ganglionectomy. The period of postoperative follow-up ranged from one month to thirty-eight months. In the patients who were improved the effect of sympathectomy persisted throughout the period of observation.

#### *Results of Lumbar Ganglionectomy in Nineteen Patients*

Patient	Age	Months Followed	Result	Diabetes
I. K.....	65	11	Healed	Present
F. W.....	63	13	Healed	Absent
M. S.....	78	Amputation	Amputation	Absent
D. D.....	51	Amputation	Amputation	Present
C. F.....	53	Death 1 month after operation	Died	Present
M. W.....	73	6	Healed	Absent
A. S.....	63	6	Healed	Absent
E. F.....	53	17	Healed	Present
B. S.....	69	11	Healed	Present
I. S.....	76	16	Healed	Absent
L. C.....	62	6	Healed	Present
J. H.....	67	38	Healed	Absent
H. H.....	84	6	Healed	Present
A. A.....	70	2	Healed	Absent
M. J.....	57	Amputation	Amputation	Present
P. P.....	71	Amputation	Amputation	Absent
D. S.....	70	1	Healed	Absent
S. W.....	62	14	Healed	Present
E. S.....	62	8	Healed	Present

In 14 of the cases the denervation produced an improvement, with healing of the necrotic area. In the remaining 5 cases failure was evidenced by the progression of the necrosis, which made amputation necessary.

Sympathetic block with procaine hydrochloride was used routinely. Though in most cases the injection indicated the expected operative effect, it was not uniformly dependable. It was our conclusion that a negative effect of sympathetic block did not necessarily indicate that there would be failure. This fact certainly undermines the value of preoperative injection of procaine hydrochloride as a test.

Though 9, or 48 per cent, of our patients had diabetes, there seemed to be no specific relationship between the result obtained and the presence or absence of diabetes, as indicated in the accompanying table which summarizes the results.

## CONCLUSIONS

It is difficult to draw accurate conclusions from the clinical study of small groups of patients when controls cannot properly be established. Consequently, despite careful study of these cases, we can only state that the enucleation of the second and third lumbar ganglions with the intervening sympathetic trunk produced improvement in 73 per cent of patients with late manifestations of arteriosclerosis. In the remaining 27 per cent the procedure failed to influence the necrotic process. To interpret the degree of improvement in the patients who benefited is most difficult. Therefore, we have simply considered as improvement the healing of the necrotic process with or without minimal loss of tissue, as in amputation of a toe with healing of the stump. The accompanying increase in the temperature of the skin and the decrease in pain have evaded satisfactory comparative interpretation.

The employment of sympathectomy in cases in which major amputation is required may allow for an occasional amputation below the knee. However, in the large majority of cases in which amputation must ensue despite sympathectomy the supracondylar procedure becomes imperative.

Further studies are needed to establish adequate controls for clinical impressions. In addition, there is a crying need for the establishment of criteria of indications and contraindications for lumbar sympathectomy. Adequate standardization will be arrived at when a series of cases sufficiently large to be statistically important can be studied.

# SURGICAL CONSIDERATIONS IN HEMORRHAGE OF THE UPPER PART OF THE GASTROINTESTINAL TRACT

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THE OCCURRENCE of massive hemorrhage from the stomach or the upper part of the small bowel presents a difficult problem to the clinician. A diagnostic problem is immediately presented because of the great variety of conditions which may produce such bleeding. A therapeutic problem is raised because of the lack of specific measures available for control of such hemorrhage and because of the existing differences of opinion regarding the proper treatment.

The existence of differences of opinion regarding the treatment of hemorrhage from the upper part of the gastrointestinal tract, especially in regard to the indications for surgical intervention in patients with bleeding peptic ulcer, has prompted us to report our experience with cases in a large charity institution.

## MATERIAL

A total of 305 patients was studied, who entered the Cook County Hospital because of gross melena, hematemesis or both. These patients were admitted during the three year period from 1943 to 1945 inclusive. In each instance the hemorrhage constituted the chief complaint.

The patients included in the present study represent a group with rather severe conditions, as is indicated by the fact that 40 per cent had a red blood cell count below 2,500,000 on their admission and 26 per cent had fainted as a result of their bleeding.

Of the 305 patients, 230 had bleeding from a gastroduodenal ulcer, while 75 bled from nonpeptic ulcer or from extragastric causes.

## SEX, RACE AND AGE DISTRIBUTION

In this series bleeding from the upper part of the gastrointestinal tract occurred much more commonly in men than in women. In the 230 cases of bleeding peptic ulcer 83.5 per cent of the patients were men and 16.5

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per cent women. Of the 75 patients without ulcers, 78.7 per cent were men and 21.8 per cent women (table 1).

Of the patients with ulcer, 176 were white, 52 were Negroes, 1 was Chinese and 1 Japanese. In the group of patients without ulcers there were 62 white persons and 13 Negroes (table 2).

The patients with bleeding peptic ulcer ranged in age from 20 to 83 years. Fifty-eight per cent were between the ages of 40 and 60. The patients without ulcer had a somewhat higher average age, the range being from 20 to 80 years and 77.3 per cent being between the ages of 40 and 70 (table 3).

TABLE 1.—*Sex Distribution in 305 Cases of Bleeding in the Upper Part of the Gastrointestinal Tract*

Sex	Ulcer		No Ulcer	
	Number of Cases	Percentage	Number of Cases	Percentage
Male.....	192	83.5	59	78.7
Female.....	38	16.5	16	21.3

TABLE 2.—*Race Distribution*

Race	Ulcer		No Ulcer	
	Number of Cases	Percentage	Number of Cases	Percentage
White.....	176	76.4	62	82.7
Negro.....	52	22.74	13	17.3
Chinese.....	1	0.43	0	0
Japanese.....	1	0.43	0	0

#### CAUSE OF BLEEDING IN THE UPPER PART OF THE GASTROINTESTINAL TRACT

In the 305 cases studied there were 11 different diagnoses made of the cause of bleeding, and in 7 cases the source of bleeding could not be determined with any degree of certainty (table 4).

A diagnosis of bleeding peptic ulcer was made in 230, or 75.6 per cent, of the cases. The site of the ulcer was determined in 46.8 per cent of the patients, being duodenal in 58 per cent, gastric in 27.4, marginal in 10 and both gastric and duodenal in 4.6.

Bleeding esophageal varices due to portal cirrhosis of the liver was the diagnosis second in frequency, with an incidence of 9.8 per cent. A diagnosis of acute gastritis was made for 5.1 per cent of the patients. Carcinoma of the stomach was next in frequency and accounted for 4.9 per cent of the cases in which there was bleeding. There was 1



case each of the following conditions: polyp of the stomach, carcinoma of the duodenum, primary carcinoma of the liver with thrombosis of the portal veins and bleeding esophageal varices, thrombocytopenic purpura, Banti's syndrome, syphilitic cirrhosis of the liver with bleeding esophageal varices and a large diverticulum of the duodenum in which no other source of bleeding was found.

TABLE 3.—*Age Distribution and Relation to Mortality*

Age in Years	Ulcer			No Ulcer		
	Number of Patients	Number Who Died	Mortality, Percentage	Number of Patients	Number Who Died	Mortality, Percentage
10 to 19.....	0	0	0	0	0	0
20 to 29.....	20	1	5	3	1	33.3
30 to 39.....	32	2	6.3	5	0	0
40 to 49.....	68	4	7.3	25	11	44.0
50 to 59.....	66	7	10.3	18	8	44.4
60 to 69.....	33	10	29.4	15	8	53.3
70 and over.....	11	4	36.4	9	7	77.8

TABLE 4.—*Etiologic Factors in Bleeding of the Upper Part of the Gastrointestinal Tract*

Diagnosis	Number of Cases	Percentage	Mortality, Percentage
Peptic ulcers, total.....	230	75.6	12.2
Duodenal .....	63	....	....
Gastric .....	30	....	....
Marginal .....	11	....	....
Gastric and duodenal.....	5	....	....
Site not recorded.....	121	....	....
Portal cirrhosis of the liver.....	30	9.8	63.3
Acute gastritis.....	16	5.1	5.0
Carcinoma of the stomach.....	15	4.9	60.0
Miscellaneous .....	7	2.3	71.4
Polyp of stomach.....	1	....	....
Carcinoma of duodenum.....	1 (died)	....	....
Primary carcinoma of liver with portal vein thrombosis.....	1 (died)	....	....
Thrombocytopenic purpura.....	1 (died)	....	....
Banti's syndrome.....	1 (died)	....	....
Syphilitic cirrhosis of liver.....	1 (died)	....	....
Diverticulum of duodenum.....	1	....	....
Diagnosis undetermined.....	7	2.3	....

There are a number of other conditions which may produce hematemesis or melena but which were not encountered in this series. Among these are hiatus hernia, tumors or diverticula of the small bowel, benign tumors of the stomach (especially leiomyomas) and mucosal tears in the cardia of the stomach due to violent vomiting or retching. Weiss and Mallory<sup>1</sup> have reported several fatal cases of the last condition, the chief clinical manifestations of which were persistent vomit-

1. Weiss, S., and Mallory, G. K.: Lesions of Cardiac Orifice of Stomach Produced by Vomiting, J. A. M. A. 98:1353-1355 (April 16) 1932.

ing and retching, frequently precipitated by alcoholic debauches and associated with massive hematemesis.

In 7 cases the site of the bleeding was not determined. It is often impossible to determine the cause of bleeding clinically and occasionally even at laparotomy and at necropsy. Thus Jankelson<sup>2</sup> reported a case with a long history of ulcer, two previous gastric operations and finally fatal hematemesis for which the autopsy revealed no demonstrable cause.

#### DIAGNOSIS

In making a diagnosis of peptic ulcer as the cause of bleeding, the past history is of importance. Of the 230 patients with bleeding peptic ulcer in this series, 82.4 per cent had a definite history of previous symptoms of ulcer. In only 17.6 per cent had there been no previous indication of peptic ulcer. A previous medical diagnosis had been made in 51 per cent of the cases and a previous roentgenologic diagnosis in 18 per cent. In 7 per cent of the patients a previous operation for peptic ulcer had been performed. Of the 16 patients with peptic ulcer who had undergone surgical treatment for peptic ulcer, 5 had been subjected to repair of a perforation, 7 to gastroenterostomy and 4 to gastric resection.

The roentgenogram made after a barium meal showed evidence of ulcer in 54 per cent of the 124 cases of ulcer in which such roentgenograms were recorded. In most cases barium meal studies were not done until there had been no evidence of bleeding for a period of at least ten days. The reasons for the frequency of normal roentgenograms after a barium meal following bleeding probably caused by ulcer are manifold. The ulcer might have been acute and shallow; it might have healed sufficiently to prevent barium from filling the crater; it might be in a so-called blind spot, or it might be filled with debris or blood. One of the explanations is illustrated by a case in the present series. In this case a barium meal roentgenogram made ten days after bleeding had ceased showed a normal condition. However, gastroscopy demonstrated a gastric ulcer crater which appeared to be evenly filled with a blood clot.

Gastroscopy is an important aid in determining the site of bleeding. It was performed in 30 of the patients with peptic ulcer and demonstrated the ulcer in 8. In each of the 8 cases the ulcer was of the gastric type. In 1 additional case intense gastritis indicative of a stomal ulcer was seen at the gastroenterostomy opening. In 4 cases gastroscopy revealed an ulcer which escaped detection by the roentgenogram made after a barium meal. In 2 cases gastroscopy gave negative results and roentgenologic study revealed gastric ulcer (table 5). These findings indicate that both barium meal studies and gastroscopy should be

2. Jankelson, I. R.: *Gastroenterology* 9:472-475, 1947.

done in cases of bleeding of the upper part of the gastrointestinal tract in order to locate the site of the bleeding in the greatest number of patients possible.

The diagnosis of portal cirrhosis with bleeding from esophageal varicosities was in most cases made clinically on the basis of signs of advanced disease of the liver. Palpable enlargement of the liver was recorded in 60 per cent of the 30 cases of cirrhosis of the liver. Ascites was present in 30 per cent, edema of the extremities in 13 per cent, dilated superficial abdominal veins in 16.6 per cent, palpable spleen in 10 per cent and jaundice in 3.3 per cent. Patients with melena alone are unlikely to be bleeding from esophageal varicosities. In this series of cases all 30 with portal cirrhosis of the liver had hematemesis. In contrast, 24 per cent of the patients with bleeding peptic ulcer had only melena.

TABLE 5.—*Results of Gastroscopy in 30 Cases of Bleeding Peptic Ulcer*

Final Diagnosis	Number of Cases	Gastroscopy		Roentgenologic Study	
		Positive Results	Negative Results	Positive Results	Negative Results
Gastric ulcer.....	10	8	2	6	4
Duodenal ulcer.....	9	0	9	9	0
Marginal ulcer.....	1	1*	0	0	1
Peptic ulcer by clinical diagnosis and previous roentgenologic study.....	10	0	10	0	10

\* Intense gastritis at the stoma was present.

The importance of gastritis as a cause of bleeding has been demonstrated by Benedict<sup>3</sup> and others. Benedict also pointed out the frequent association of gastritis with duodenal ulcer and the difficulty of determining in such cases whether the bleeding is coming from the ulcer or the gastritis.

A diagnosis of gastritis in the absence of gastroscopy is not definite. Of the 16 patients with gastritis in our series, only 7 were given gastroscopic examination. Of these, 3 showed multiple shallow gastric erosions with bleeding, 2 showed hypertrophic gastritis with pseudopolypi and 2 showed atrophic gastritis. The remaining patients belong to a group seen at Cook County Hospital who present themselves after an alcoholic debauch with symptoms of epigastric pain and vomiting of blood and who have no history or symptoms suggestive of peptic ulcer or of other known causes of bleeding of the upper part of the gastrointestinal tract.

As has been shown, peptic ulcer, portal cirrhosis of the liver, acute gastritis and carcinoma of the stomach are the most common causes

3. Benedict, E. B.: *Am. J. Roentgenol.* **47**:254-261, 1942.

of this condition. The seven rarer causes of bleeding represented in this series illustrate the importance of careful examination and laboratory study of patients with hematemesis or melena.

The patient with bleeding from a polyp of the stomach was a 66 year old man who entered the hospital in shock with a blood pressure of 96 systolic and 40 diastolic after having hematemesis and melena for three days. The diagnosis was made by gastroscopy after two barium meal roentgenograms had shown no abnormality. The diagnosis of carcinoma of the duodenum was made at operation, at which time a gastroenterostomy was done for the relief of obstruction.

The patient with carcinoma of the liver and thrombosis of the portal veins presented the picture of drowsiness, coma, jaundice, hematemesis and oliguria. Spider telangiectases were noted, and the clinical diagnosis of acute yellow atrophy of the liver was considered. The final diagnosis was made at autopsy. Retrograde thrombosis of the portal veins arising in an area of primary carcinoma of the liver and bleeding esophageal varices were found.

The case of Banti's syndrome involved a 20 year old youth who had long-standing splenomegaly and who, in addition to massive hematemesis, had enlargement of the liver, ascites and anemia. At autopsy old thrombosis of the portal veins with cirrhosis of the liver and enlargement and fibrosis of the spleen were found.

The diagnosis of thrombocytopenic purpura was made for a 40 year old woman, who in addition to having hematemesis and melena had had a missed abortion. She had a platelet count of 1,200, a prolonged bleeding time and a normal clotting time, and sternal biopsy revealed signs compatible with the diagnosis of thrombocytopenic purpura. This patient died thirty days after splenectomy.

The diagnosis of syphilitic cirrhosis of the liver with bleeding esophageal varices was made at autopsy on a 56 year old man for whom a clinical diagnosis of bleeding peptic ulcer had been made. At post-mortem examination a healed duodenal ulcer was found in addition to syphilitic cirrhosis and bleeding esophageal varices. This case illustrates the fact that a history of peptic ulcer and a deformed duodenal bulb do not always mean that an ulcer is the cause of the bleeding.

The patient with possible bleeding from a duodenal diverticulum was a 69 year old man with no past history of gastrointestinal complaints who entered the hospital after vomiting dark bloody material six times in three days and having tarry stools for three days. The blood pressure on admission was 164 systolic and 94 diastolic, and the red blood cell count was 2,500,000. The only positive finding was a large diverticulum of the second portion of the duodenum demonstrated by the roentgenogram made after a barium meal. The patient received two blood transfusions and made an uneventful recovery.

PROGNOSIS OF BLEEDING IN THE UPPER PART OF THE  
GASTROINTESTINAL TRACT

The mortality associated with the various causes of bleeding found in our series of patients is shown in table 4. It can be seen that the over-all mortality for patients with bleeding peptic ulcer was 12.2 per cent.

Bleeding from esophageal varices due to portal cirrhosis of the liver had a high mortality, 63.3 per cent. Various methods of therapy for such hemorrhage have been advocated. The injection of sclerosing solutions into the varicosities has been used by Moersch,<sup>4</sup> Patterson and Rouse,<sup>5</sup> Welt and Blatteis<sup>6</sup> and others. However, temporary arrest of hemorrhage is the most that can be expected as long as the underlying portal hypertension is present. Recently Rowntree<sup>7</sup> and his associates have described a method of employing internal venous tamponage in the esophagus by means of a latex bag inflated in the esophagus. Som and Garlock<sup>8</sup> have recently described another method, which involves the performance of posterior mediastinotomy to create a new collateral circulation between the submucosal and periesophageal veins of the esophagus and the deeper veins of the mediastinum. The surgical establishment of a portacaval shunt, as developed by Whipple<sup>9</sup> and Blakemore and Lord,<sup>10</sup> is effective in reducing portal hypertension caused by portal cirrhosis of the liver. Phemister<sup>11</sup> has emphasized the importance of varicosities in the cardia of the stomach which may accompany esophageal varices and produce hemorrhage; he describes a method for the surgical treatment of esophageal varices by esophagogastric resection. The high mortality from bleeding of esophageal varicosities certainly justifies radical attempts at treatment.

The mortality rate for the patients with gastritis who had bleeding was 5 per cent. The hospital mortality rate among the patients with bleeding from carcinoma of the stomach was 60 per cent. Of the 7 patients with other more rare causes of bleeding, 5 died. Of the 7 patients with bleeding of undetermined origin, 2 died.

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4. Moersch, H. J.: *J. Thoracic Surg.* **10**:300-309, 1941.

5. Patterson, C. O., and Rouse, M. O.: *Injection Treatment of Esophageal Varices*, *J. A. M. A.* **130**:384-386 (Feb. 16), 1946.

6. Welt, B., and Blatteis, S. R.: *Am. J. Surg.* **63**:415-417, 1944.

7. Rowntree, L. G.; Zimmerman, E. F.; Todd, M. H., and Ajac, J.: *Intra-esophageal Venous Tamponage: Its Use in Case of Varical Hemorrhage from Esophagus*, *J. A. M. A.* **135**:630-631 (Nov. 8) 1947.

8. Som, M. L., and Garlock, J. H.: *New Approach to Treatment of Esophageal Varices*, *J. A. M. A.* **135**:628-629 (Nov. 8) 1947.

9. Whipple, A. O.: *Ann. Surg.* **122**:449-475, 1945.

10. Blakemore, A. H., and Lord, J. W., Jr.: *Ann. Surg.* **122**:476-489, 1945.

11. Phemister, D. B., and Humphreys, W. M.: *Ann. Surg.* **126**:397-410, 1947.

FACTORS RELATED TO THE PROGNOSIS FOR PATIENTS WITH  
BLEEDING PEPTIC ULCER

The foregoing paragraphs have emphasized the variety of conditions which can produce melena or hematemesis. It can be seen that many of these conditions cannot be benefited by surgical treatment and that, therefore, when an operation to stop bleeding is being considered a fairly definite diagnosis of the source of the bleeding must first be made. In the consideration of surgical intervention, it is also of importance to be able to estimate a given patient's chances to survive under medical treatment.

Age is one of the factors having the greatest effect on the mortality of bleeding peptic ulcer. Table 3 shows that in the present series there was a progressive increase in mortality with increasing age. There were 120 patients under the age of 50, of whom 7 died, a mortality rate of 5.8 per cent. There were 110 patients over the age of 50, of

TABLE 6.—*Relation of Number of Previous Hemorrhages to Mortality*

Number of Previous Hemorrhages	Ulcer			No Ulcer		
	Number of Patients	Number Who Died	Mortality, Percentage	Number of Patients	Number Who Died	Mortality, Percentage
0.....	140	12	9.2	55	28	50.9
1.....	56	9	15.8	13	3	23.1
2.....	8	3	37.5	5	3	60.0
3.....	9	1	11.1	0	0	0
4 or more.....	17	2	12.8	2	0	0

whom 21 died, a rate of 19.1 per cent. The sharpest rise in mortality occurred at about the age of 60. Of the 44 patients over the age of 60, 14 died, a mortality rate of 31.8 per cent.

The number of previous hemorrhages has often been shown to be a factor influencing the mortality of bleeding peptic ulcer. In the present series the relation between the number of previous hemorrhages and mortality was not striking (table 6). There were not enough patients with more than one previous episode of bleeding to make the figures statistically significant. However, it may be seen that the mortality rate among 142 patients who were having their first episode of bleeding was 9.2 per cent, whereas that among the 106 patients with previous bleeding was 15.8 per cent.

Certain symptoms seemed to be related to an increase in mortality. Among the 47 patients having fainting as a symptom there was a mortality rate of 21.3 per cent as compared to 12 per cent for the entire group of patients with bleeding peptic ulcer. Pain in the back was complained of by 7 patients, and of these, 2 died. It is known that a posterior penetrating ulcer which erodes the gastroduodenal or the superior

pancreaticoduodenal artery is one of the common sources of bleeding which continues in spite of medical treatment, and therefore pain in the back might be expected to indicate an intractable type of bleeding. Diarrhea was present in 32 patients, 18.7 per cent of whom died. It is logical that the mortality rate among patients having enough bleeding into the gastrointestinal tract to produce a bloody diarrhea should be higher than the average.

TABLE 7.—*Relation of Blood Pressure on Admission to Mortality in 286 Cases of Bleeding of the Upper Part of the Gastrointestinal Tract*

Blood Pressure	Ulcer			No Ulcer		
	Number of Cases	Deaths	Mortality, Percentage	Number of Cases	Deaths	Mortality, Percentage
Normal, systolic 100 to 150, diastolic 60 to 90.	178	15	8.4	52	25	48
Low, systolic, 90 or below .....	43	16	37.2	6	6	75
High, systolic over 170, diastolic over 90.....	4	0	0	1	1	100

TABLE 8.—*Relation of Red Blood Cell Count on Admission to Mortality*

Red Blood Cell Count	Ulcer			No Ulcer		
	Number of Cases	Deaths	Mortality, Percentage	Number of Cases	Deaths	Mortality, Percentage
4,500,000.....	20	2*	10	5	2	40
4,000,000 to 4,500,000.....	20	1	5	7	1	14.3
3,500,000 to 4,000,000.....	28	0	0	9	2	22
3,000,000 to 3,500,000.....	31	2	6.5	10	5	50
2,500,000 to 3,000,000.....	33	1	3.0	9	8	88
2,000,000 to 2,500,000.....	35	7	20	6	2	33.3
1,500,000 to 2,000,000.....	35	6	17.1	5	3	60
1,000,000 to 1,500,000.....	14	3	21.4	3	2	66.6
Below 1,000,000.....	4	2	50	0	..	....

\* In 1 case the red blood cell count dropped to 1,600,000 and operation was performed.

The blood pressure on admission gives some indication of the severity of the bleeding and of the mortality to be expected (table 7). Among the 178 patients with a systolic blood pressure of 100 or above the mortality was 8.4 per cent, whereas in the 43 patients with a systolic blood pressure below 100 the mortality was 37.2 per cent. There were only 4 patients in the series who had hypertension on admission, and in this group there were no deaths. A definite correlation was found between the red blood cell count on admission and the mortality, as is shown in table 8.

A relation was found between the blood nonprotein nitrogen level and the mortality of bleeding peptic ulcer (table 9). In the 78 patients

with a nonprotein nitrogen level of 50 or below there was a mortality of 2.6 per cent, while in the 32 patients with a level between 50 and 100 there was a mortality of 12.5 per cent. There were only 2 cases in which a determination of the nonprotein nitrogen showed a value over 100, and both of the patients died. In almost all instances in which the nonprotein nitrogen was increased the creatinine level of the blood was normal or only slightly above it. It is known that free blood in the gastrointestinal tract will produce an increased blood nonprotein nitrogen content. This has been demonstrated experimentally by Kaump and Parsons.<sup>12</sup> Schiff<sup>13</sup> and his associates have shown that digestion of blood from the gastrointestinal tract leads to an increase of the blood urea nitrogen which is proportional to the amount of blood in the bowel. They also showed that the blood urea nitrogen level remains increased for only twenty-four to thirty-six hours from one episode of bleeding. These findings suggest that repeated determina-

TABLE 9.—*Relation of Nonprotein Nitrogen Level on Admission to Mortality in 140 Cases of Bleeding of the Upper Part of the Gastrointestinal Tract*

Nonprotein Nitrogen	Ulcer			No Ulcer		
	Number of Cases	Deaths	Mortality, Percentage	Number of Cases	Deaths	Mortality, Percentage
50 or below.....	78	2	2.6	18	6	33.3
50 to 100.....	32	4	12.5	10	5	50.0
Over 100.....	2	2	100.0	0	0	0

tions of the blood urea nitrogen level are of value in estimating recurrence of bleeding from a peptic ulcer and that this method should be used more often. Persistent high levels of nonprotein nitrogen may also result from damage to the kidney during the period of shock from the initial severe bleeding.

In determining the prognosis for a patient with a bleeding peptic ulcer the response to a short trial of medical treatment is of great importance. In the group of patients in this series it was apparent that the prognosis for those who continued to bleed or had a recurrence of bleeding after forty-eight hours of medical treatment was poor. There were 14 such patients who were treated medically, and 8 died, a mortality of 58 per cent. Fifteen patients who continued to bleed or had recurrence of bleeding after forty-eight hours of medical treatment were operated on, and of these, 5 died, a mortality rate of 30 per cent (table 10).

12. Kaump, O. H., and Parsons, J. C.: *Am. J. Digest. Dis.* 7:191-194, 1940.

13. Schiff, L.; Stevens, R. J., and Mass, H. K.: *Am. J. Digest. Dis.* 9:110-113, 1942.



Heuer<sup>14</sup> stated that in differentiating patients with fatal and non-fatal types of hemorrhage the most important criterion is the failure to improve promptly under a strict medical regimen. He, moreover, expressed the belief that if surgical intervention is chosen it should be done within the first twenty-four to forty-eight hours after the onset of the hemorrhage. The importance of early operation was originally stressed by Finsterer,<sup>15</sup> Gordon-Taylor<sup>16</sup> and Allen.<sup>17</sup> Since in most instances it is difficult to determine which patients will not respond to medical treatment in less than forty-eight hours, it would seem to us that most of the emergency operations should be performed between forty-eight and seventy-two hours after the onset of the bleeding, although earlier surgical intervention may be necessary in rare cases. In some patients the presence of an associated complication, e. g., obstruction, large crater or intractable pain, may influence the decision to intervene surgically. Patients who apparently stop bleeding during

TABLE 10.—*Course of 29 Patients with Bleeding Peptic Ulcer Who Continued to Bleed or Had Recurrence of Bleeding After Forty-Eight Hours of Treatment on Medical and Surgical Regimen*

Type of Treatment	Number of Patients	Number Who Died	Mortality, Percentage
Medical treatment.....	14	8	57.8
Surgical treatment.....	15	5	33.0

the first forty-eight hours of medical treatment and then have a recurrence of massive bleeding four or five days later are also candidates for surgery, since their prognosis under medical treatment is poor.

The fact that in the present series of cases 50 per cent of the fatalities occurred during the first three days in the hospital is another indication that an early decision regarding surgical intervention should be made.

#### RESULTS IN MEDICALLY TREATED PATIENTS WITH BLEEDING PEPTIC ULCER

The mortality rate among 204 patients with bleeding peptic ulcer treated medically was 11.3 per cent. Of the 14 patients who continued to bleed or had recurrence of bleeding after forty-eight hours of medical treatment and who were not operated on, 8 died, a mortality rate of 58 per cent.

14. Heuer, G. J.: *New England J. Med.* **235**:777-783, 1946.
15. Finsterer, H.: *Lancet*: **2**:303-305, 1936.
16. Gordon-Taylor, G.: *Brit. J. Surg.* **33**:336-345, 1946.
17. Allen, A. W.: *Surgery* **2**:713-731, 1937.

RESULTS IN SURGICALLY TREATED PATIENTS WITH  
BLEEDING PEPTIC ULCER

In any discussion of the operative treatment of patients with bleeding peptic ulcer it is essential to distinguish between surgical procedures performed during active bleeding and those performed after bleeding has ceased. As is shown by others<sup>18</sup> and by our series, emergency surgical intervention during active bleeding carries an appreciable mortality and should be reserved for only a few carefully selected patients, whereas an interval operation can be done with a low mortality.

A number of difficulties may be encountered in operations on the actively bleeding patient. The patient may have been in shock or in impending shock and for that reason may be unable to tolerate surgical intervention well. The diagnosis of the source of bleeding may not be definite. There may be multiple bleeding points in the stomach and duodenum. It may be difficult to find the bleeding point in a

TABLE 11.—*Indications for Surgical Intervention in 26 Patients with Bleeding Peptic Ulcer*

Indication	Number of Patients	Number Who Died
Emergency operation for continuing bleeding.....	10	5
Interval operation because of repeated bleeding.....	5	0
Interval operation for complications other than bleeding.....	11	0

blood-filled stomach, especially if it is high on the lesser curvature. Bleeding may recur postoperatively after ligation or suture of a bleeding ulcer. All these difficulties were encountered among the 26 surgically treated patients in this series.

The over-all mortality in the 26 surgically treated patients was 19.2 per cent, as compared with 11.3 per cent for the 204 medically treated patients.

In 10 patients an emergency operation during active bleeding was performed, and of these, 5 died. In 5 patients operation was performed after initial bleeding had ceased because of repeated episodes and the danger of further bleeding, and in this group there were no deaths. In 11 patients operation was performed after bleeding had ceased, chiefly because of complications other than bleeding, and in this group there were no deaths. It can be seen that an interval operation is preferable whenever possible (table 11).

In the 26 surgically treated patients the condition was much more severe and intractable than in the medically treated patients (table 12).

18. Metheney, D., and Green, D. M.: West. J. Surg. 55:97-102, 1947. Allen,<sup>17</sup> Gordon-Taylor.<sup>16</sup>

The average age was about the same for both groups, 50 for the medically treated and 48 for the surgically treated patients. The surgically treated patients had a higher number of previous episodes of bleeding, a mean of 1.5 as compared to a mean of 0.63 for the medically treated patients. The surgically treated group had an incidence of complications of ulcer other than bleeding of 92 per cent, as compared to 30 per cent for the medically treated patients (table 13). Of the surgically treated patients, 58 per cent had continued to bleed or had recurrence of bleeding after forty-eight hours of medical treatment, whereas only

TABLE 12.—*Comparison of Clinical Data on Medically and Surgically Treated Patients with Bleeding Peptic Ulcer*

Type of Treatment	Number of Cases	Average Age	Average Number of Previous Bleeding Episodes	Incidence of Complications Other than Bleeding, Percentage	Mortality, Percentage
Medical.....	204	50	0.63	30	11.3
Surgical.....	26	48	1.5	92	19.2

TABLE 13.—*Complications Other than Bleeding in 26 Surgically Treated Patients with Peptic Ulcer*

Complication	Number of Cases	Percentage
Intractability.....	14	56
Obstruction.....	6	24
Perforation.....	1	4
Gastric type.....	6	24
Marginal type.....	1	4
Continuing massive hemorrhage.....	10	36

7 per cent of the medically treated patients showed evidence of bleeding after forty-eight hours of treatment.

Table 14 shows the types of operations performed and the results of each type. Of the patients operated on during active bleeding, 7 underwent gastric resection, with 2 deaths, 2 were subjected to suture of the ulcer and gastroenterostomy and both died from continued hemorrhage and 1 patient underwent duodenotomy and gastrotomy without the bleeding point being found. This patient continued to bleed post-operatively and died, and at autopsy a gastric ulcer was found. Among the patients operated on after active bleeding had ceased, 15 underwent gastric resection, with no deaths, and 1 underwent separation of a penetrating ulcer from the liver, suture of the opening in the stomach and gastroenterostomy. This patient also recovered.

In the 10 patients operated on during active bleeding gastric resection was more successful than attempts to control a bleeding point by suture or ligation. It would seem that a gastric resection is the operation of choice, unless the patient is too poor an operative risk.

Table 15 gives an analysis of the 5 deaths in the surgically treated patients and shows that in 3 cases death occurred from continued

TABLE 14.—*Results of Different Types of Operation in 26 Surgically Treated Patients with Peptic Ulcer*

Type of Operation	Actively Bleeding at Time of Operation		Interval Operation	
	Number of Patients	Number Who Died	Number of Patients	Number Who Died
Gastric resection.....	7	2	15	0
Suture of ulcer and gastroenterostomy.....	2	2	1	0
Duodenotomy and gastrotomy.....	1*	1	0	0

\* No bleeding point was found. Bleeding continued postoperatively, and a gastric ulcer was found at autopsy.

TABLE 15.—*Analysis of Fatalities in Surgically Treated Patients with Bleeding Peptic Ulcer\**

Age	Time of Death		Type of Operation	Cause of Death	Post- mortem Examina- tion
	Number of Days After Admis- sion	Number of Days After Opera- tion			
53.....	8	4	Gastrotomy and duodenotomy; no bleeding point found	Massive hemorrhage; continued bleeding from gastric ulcer	Yes
24.....	52	5	Gastric resection	Atelectasis; trans- fusion reaction	No
49.....	29	10	Ligation of vessel in duodenal ulcer; gastroenterostomy	Continued bleeding; peritonitis from leak- ing suture line	Yes
51.....	42	3	Perforation into liver closed; gastro- enterostomy	Continued bleeding	No
60.....	12	4	Gastric resection	Atelectasis and pneumonia	No

\* Of the 5 patients who died, 3 had red blood cell counts below 1,500,000 on their admission to the hospital. In the other 2 there was a sharp drop in the red blood cell count while they were in the hospital, to 2,100,000 in 1 and to 1,600,000 in the other.

massive hemorrhage postoperatively. In 1 of these 3 patients peritonitis from a leaking suture line contributed to the fatal result. In all 3 of the patients who continued to bleed postoperatively an attempt to treat the bleeding ulcer by ligation or suture had been made. In the other 2 fatal cases postoperative complications were responsible for death. One of the 2 patients had atelectasis and a severe transfusion

reaction. The other had atelectasis and superimposed pneumonitis. The 5 deaths occurred between the third and the tenth postoperative day.

All 5 of the patients who died after surgical intervention were severely ill. Three were operated on after a week or more of medical treatment with bleeding still continuing or recurring. Three had red blood cell counts below 1,500,000 on their admission to the hospital, and the other 2 had a sudden drop in the red blood cell count in the hospital under medical treatment, i. e., in one to 2,100,000 and in the other to 1,600,000.

#### COMMENT

The management of patients with massive hemorrhage from the upper gastrointestinal tract presents a difficult problem, from the point of view of both diagnosis and therapy. Thus in the 305 patients of our series 11 different causes for the bleeding were encountered, and in a small group no cause was found at all. The therapeutic considerations must take into account not only the gastrointestinal tract, in which the bleeding is manifest, but also a number of extragastrointestinal factors. In elderly persons, especially, who when they have gastrointestinal bleeding present difficult problems *a priori*, other factors relating to the cardiovascular, genitourinary and pulmonary system must be strongly considered.

Intensive medical management must be started in every patient with massive bleeding from the upper part of the gastrointestinal tract. This should consist of absolute rest in bed, sedation, blood transfusions and the administration of other fluids to restore the patient's electrolyte balance and to combat dehydration and azotemia. Vitamins and antispasmodics can be given parenterally. If vomiting has ceased shortly after the patient enters the hospital, one of the many antacids may be given with the hourly milk and cream feedings.

Blood transfusions, repeatedly given if necessary, are the basis for successful treatment of bleeding ulcers. While there still exist some who object to the use of blood transfusions because they may cause further bleeding due to sudden elevation of the blood pressure, the majority of clinicians favor transfusions. Some,<sup>19</sup> including ourselves, advocate massive blood transfusions or rather sufficient blood to replace the amounts lost by hematemesis or melena. Others<sup>20</sup> recommend the

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19. (a) Bockus, H. L.: *Gastroenterology*, Philadelphia, W. B. Saunders Company, 1946, vol. 1, chap. 29. (b) Gray, S. J.: *M. Clin. N. America* **31**:1121-1134, 1947. (c) Miller, T. G., and Elsom, K. A.: *M. Clin. N. America* **22**:1711-1733, 1938.

20. Crohn, B. B., and Lerner, H. H.: *Am. J. Digest. Dis.* **6**:15-22, 1939. Kirsner, J. B., and Palmer, W. L.: *Internat. Clin.* **4**:105-126, 1939. Marriott, H. L., and Kekwick, H.: *Lancet* **1**:977-981, 1935. Wood, I. J.: *M. J. Australia* **2**:1031-1038, 1937.

use of smaller transfusions. In general, we believe that the amount of blood given should be governed by the patient's need, and that, as already stated, the patient receiving blood should be carefully watched for other symptoms and signs which might indicate a possible overburdening of the cardiovascular system. When the blood is given slowly (about 4 cc. per minute) and only to patients for whom it is definitely indicated, there is little need to fear further bleeding caused by a rise in blood pressure. Blood transfusions are of value not only because they restore the patient's blood volume but also because they combat hypoproteinemia and improve his general condition.

Most clinicians believe that the treatment of choice for the great majority of patients with acute massive hemorrhage from a peptic ulcer of the stomach or duodenum is medical management. There are, however, instances in which such a hemorrhage may prove fatal unless surgical intervention is performed. Such possibilities are more likely to occur in patients over 45 or 50 years of age. We feel that for patients with peptic ulcers who continue to show evidence of active bleeding, despite intensive medical management, surgical intervention must be seriously considered at any time after their admission<sup>21</sup> and that it should not be delayed until the patient becomes too poor a surgical risk.<sup>22</sup> A similar attitude is also expressed by others,<sup>23</sup> but this opinion is not uniformly held.

There are, however, factors which must be weighed against the indications in each individual case. The presence of cardiac decompensation, of renal disease or of some other associated severe extra-gastrointestinal illness may suggest giving the medical regimen a somewhat longer trial. Similarly, marked obesity, severe hypertension and cerebral manifestations may speak against early surgical intervention. Occasionally the lack of definite knowledge of the source of bleeding will influence the decision concerning immediate operation.

#### SUMMARY AND CONCLUSIONS

A group of 305 patients admitted to the Cook County Hospital because of hemorrhage of the upper part of the gastrointestinal tract were studied. Data are presented concerning (a) the differentiation of bleeding ulcer from other causes of gastrointestinal hemorrhage; (b) factors influencing the course, and (c) factors indicating surgical intervention and results. On the basis of these data the following conclusions can be drawn:

21. Meyer, K. A., and Steigmann, F.: *S. Clin. North America* **24**:29-49, 1944.

22. Goldman, L.: *Gross Hemorrhage from Peptic Ulcer: Its Morbidity, Mortality and Treatment*, *J. A. M. A.* **107**:1537-1542 (Nov. 7) 1936.

23. Kruse, F. H.: *Complications of Peptic Ulcer and Their Treatment*, *J. A. M. A.* **109**:868-874 (Sept. 11) 1937. Finsterer,<sup>15</sup> Gray,<sup>19b</sup> Heuer.<sup>14</sup>

1. Hematemesis or melena may be produced by a variety of conditions. In making a diagnosis of the cause of bleeding careful elicitation of the history and examination are important, as are roentgenologic studies after a barium meal, gastroscopy, liver function tests, serologic studies, a search for lesions of the small bowel and a search for possible blood dyscrasias.

2. Various factors affect directly the prognosis for patients with bleeding peptic ulcer. Among these are the age of the patient, the number of previous hemorrhages, the blood count and blood pressure on admission to the hospital, the blood nonprotein nitrogen, the presence of certain symptoms such as fainting and the response to a trial of medical treatment.

3. The majority of patients with bleeding peptic ulcer can best be treated medically, and adequate amounts of blood are important in this treatment.

4. The prognosis for patients who continue to bleed actively while under an intensive medical regimen or who have a recurrence of bleeding after forty-eight hours of medical treatment is poor. In our series the mortality rate among such patients was 58 per cent on continued medical treatment as compared to 30 per cent with surgical intervention. Therefore as a group these patients seem to have a better chance with surgical treatment.

5. Surgical intervention during active bleeding from a peptic ulcer carries a high mortality and should be reserved for a small group of carefully selected patients. The chief indication is the failure of bleeding to stop within forty-eight hours under medical treatment or its recurrence during medical treatment, especially in patients over 45 years of age.

6. If the patient is not in too poor condition, a gastric resection is the operation of choice.

7. Many patients for whom the prognosis is poor because of their age or the number of previous hemorrhages or who have bled repeatedly in spite of medical treatment should be operated on between episodes of bleeding after proper preparation. The mortality rate can be kept low, and in most cases operation will prevent further hemorrhages.

## RESECTION OF THE INTERVERTEBRAL DISK THROUGH THE POSTERIOR APPROACH

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IN A PREVIOUS paper it was shown that fusion of the vertebral bodies could be attained when the intervertebral disk was removed through the transabdominal approach.<sup>1</sup> It was predicated at that time that the same result could be obtained by removing the disk after a laminectomy from the usual posterior approach. It has been claimed by some surgeons that osseous union will be secured in patients after thorough removal of the disk through the posterior approach, although no conclusive evidence has been presented to establish it as a fact.

In order to study the results of a resection of the disk through the posterior approach, a series of experiments were performed on animals. The method employed consisted of exposing the spinous processes and the laminae of the lower lumbar vertebrae. Because of the small size of the laminae and the disk, it was necessary to remove the spinous processes to obtain sufficient exposure and room to see the disk. Furthermore the disk is small in the dog and not easily recognized through a small aperture. Seven experiments were performed on dogs at different ages, and a variable length of time was allowed to elapse before the completion of the experiment.

Dog 1 (young dog).—The duration of this experiment was one hundred and thirty-one days.

*Operation.*—An incision was made over the sixth and seventh lumbar spinous processes (the dog has seven lumbar vertebrae) and the muscle stripped off from the spinous processes and laminae subperiosteally. The spinous processes with the laminae on the right side were removed from two of the vertebrae. The cord and nerve roots were carefully deflected, and the posterior ligament was incised over the disk. The disk was then resected and curetted as thoroughly as possible. It is difficult or practically impossible to remove all the disk because of the small size of the exposure and the mechanical problems. A small metal marker was placed in the resected area to aid in identification in the roentgenograms after the operation. The wound was then closed in layers with silk. No protecting support was applied.

*Result.*—There was no motion between the sixth and seventh lumbar vertebral bodies. A slight amount of motion was seen in the articular facets on lateral

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From the Surgical Laboratory, Stanford University School of Medicine.

1. Haas, S. L.: Fusion of the Vertebrae Following Resection of the Intervertebral Disc, *J. Bone & Joint Surg.* 28:544-549 (July) 1946.



bending. There was some regeneration of bone in the region of the resected laminae. The disk from the anterior side showed no evidence of bone, but as the posterior surface was approached there was a bridge of bone between the two vertebral bodies. The roentgenogram in the lateral view showed a small bridge of bone on the posterior portion of the resected disk (fig. 1A).

Dog 2 (old dog).—The duration of the experiment was one hundred and forty-six days.

*Operation.*—An incision was made over the fifth and sixth spinous processes. The laminae on the right side of the fourth and fifth lumbar vertebrae were removed, and the disk between the two was removed as thoroughly as possible. A wire marker was inserted into the disk space for identification in the roentgenogram.

*Result.*—There was only slight give between the bodies on forced pressure. There was no discernible motion at the articular facets. The disk operated on was then exposed, beginning from the abdominal side, and was found to be narrower than normal and replaced by fibrous tissue. The nucleus pulposus was only partly destroyed. The posterior part of the disk, toward the cord, was replaced by osseous tissue. The roentgenogram did not show the osseous bridge, but the disk space was narrower than normal.

Dog 3 (young full-grown dog).—The duration of the experiment was one hundred and forty-six days.

*Operation.*—The disk between the seventh lumbar vertebrae and the sacrum was exposed and destroyed as well as possible.

*Result.*—There was no evidence of fusion across the lumbosacral intervertebral disk. A small piece of bone projected upward from the sacrum toward the lumbosacral articulation. After the dissected disk was exposed some fibrous tissue was found between the bodies, which in some places looked like fibrocartilage. The laminae showed some evidence of regeneration. In the roentgenogram the disk space was found to be irregular and narrower than normal, but there was no evidence of bone bridging between the bodies.

Dog 4 (old dog).—The duration of the experiment was one hundred and forty-seven days.

*Operation.*—The disk between the seventh lumbar and first sacral segment was exposed by the same method as in the previous experiment. The disk was removed as thoroughly as possible.

*Result.*—There was no evidence of union or of restriction of motion. It was possible to get some motion in the anterior-posterior direction in the lumbosacral disk by force. The disk was widened anteriorly. Posteriorly there was some bone proliferation from the laminae of the first sacral segment. The roentgenogram showed no signs of new bone in the disk space. The disk was broader anteriorly than normal.

Dog 5 (young growing dog).—The duration of the experiment was one hundred and twenty-five days.

*Operation.*—The disk between the fifth and sixth lumbar vertebrae was resected and then curetted.

*Result.*—The laminae showed considerable evidence of regeneration. There was no motion between the fifth and sixth lumbar bodies or articular facets. The disk space was narrow, and when the area of operation was exposed, there was new bone and cartilage connecting the two bodies posteriorly. The nucleus pul-

posus was found intact. The roentgenogram shows a thin bridging with bone on the posterior side. The disk between the sixth and seventh vertebrae is thinner than normal.

Dog 6 (young growing animal).—The duration of the experiment was eighty-nine days.

*Operation.*—After the disk was exposed between the sixth and seventh lumbar bodies, it was removed by excision and curetted as thoroughly as possible.

*Result.*—There was no evidence of fixation between the two bodies. The intervertebral space was filled with soft tissue, and on manipulation there was abnormal mobility.

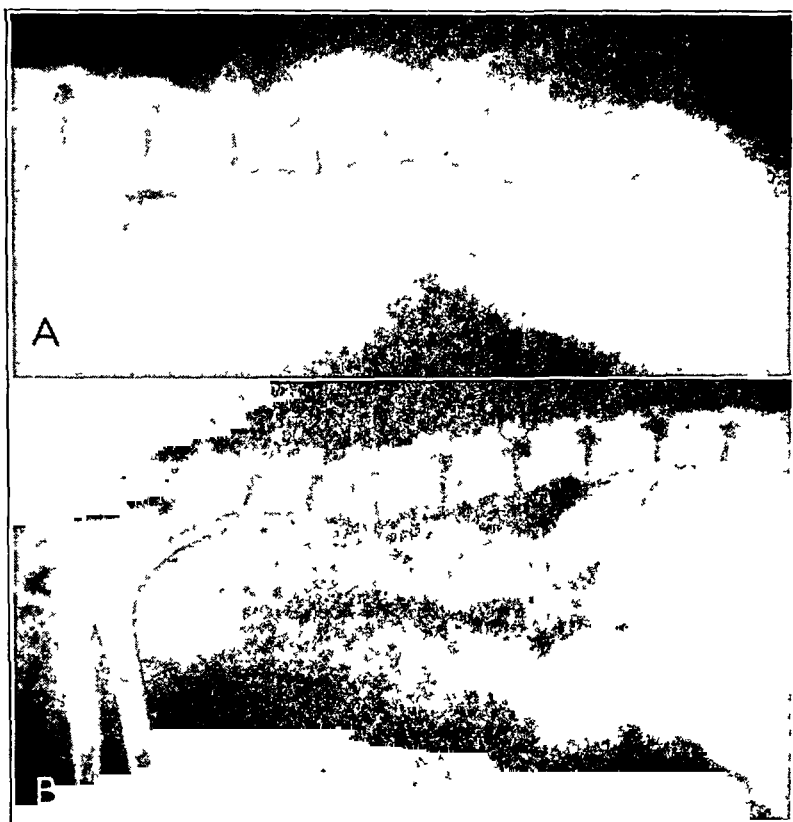


Fig. 1.—*A*, dog 1. Narrow bridge of bone on posterior portion of disk. Wire marker inserted at the time of operation. *B*, dog 8. Osseous bridge between the two vertebrae. Marker at the site of disk operated on.

There was no evidence of bone proliferation in the roentgenogram. The disk space was narrower than normal.

Dog 8 (young growing dog).—The duration of the experiment was one hundred and thirty-one days.

*Operation.*—The disk between the fifth and sixth lumbar vertebral bodies was exposed and cleaned out with a curet.

*Result.*—Good fixation was found between the fifth and sixth lumbar vertebral bodies. There was no motion between the articular facets. When a series of cuts beginning on the anterior surface were made, the anterior half of the disk was found to be replaced by fibrous tissue. About half way through an osseous

bridge was encountered extending across the intervertebral space. The laminae had partially regenerated.

The roentgenogram (fig. 1 *B*) showed a bone bridge on the posterior portion of the disk. The remainder of the disk was narrower than normal. In studying the series of roentgenograms after the operation, it was noticed that bone was not discernible until about four months postoperatively.

#### COMMENT

An osseous bridge of bone was found on the posterior or cord side of the intervertebral disk after resection. In none of the experiments was the disk entirely replaced by bone. The failure of complete union is due to the inability to remove sufficient disk tissue so as to expose bone on both vertebral bodies. This is more easily accomplished by the anterior or abdominal approach; in experiments using this approach a complete osseous bridge formed between the vertebral bodies after resection of the disk.

In several experiments there was evidence of degenerative changes after attempted resection of the disk, with increased mobility between the vertebral bodies. The failure of bone production may be due to poor regenerative powers of the bone in old animals or a failure to expose sufficient bone.

It was noticed that in the old animals there was little new bone in the intervertebral space and in most animals no new bone was found.

A period of four months was necessary after resection to be able to see bone bridging between the vertebral bodies. In no case was the entire disk replaced with bone.

When there was a bridge of bone between the bodies, firm fixation took place between them and there was no motion in the joints between the articular facets.

There was evidence of bone regeneration in the laminae after laminectomy.

#### SUMMARY

In young animals an osseous bridge was obtained between the vertebral bodies after resection of the disk by the posterior route. In no case was there a complete replacement of the disk by bone.

In old animals bone proliferation was slight. In some animals there was increased mobility at the site of the resected intervertebral disk.

An elapse of about four months was necessary before bone bridging could be seen in the roentgenogram.

## GIANT NEVUS OF THE BACK

Treated by Complete Excision and Skin Grafting

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**G**IANT moles or nevi are relatively uncommon. They are, however, generally reported as medical curiosities since, until relatively recently, they have been considered beyond the scope of ordinary treatment.

As far as I am aware, the nevus in the back to be described is one of the largest which has been excised and to have the defect closed by grafts in multiple stages.

A good review of the literature was given by Pickrell and Clay.<sup>1</sup> They also described a case of giant nevus of the thigh in a white boy aged 6 years treated by excision and immediate replacement by split-skin grafts taken from the back and the opposite thigh by means of a Padgett dermatome.

The nevus in their case measured 19 by 10 inches (48 by 25 cm.), and they described it as being the largest nevus to be excised, and to have the defect covered by skin grafts, in either single or multiple stages.

The case to be described is one in which an enormous pigmented hair-bearing nevus measuring 18 by 14 inches (45 by 35 cm.) was excised and the defect covered with grafts. The operation was done in three stages.

### REPORT OF A CASE

Mr. B., a white man aged 32, was seen in February 1944. He presented the enormous nevus on his back, the measurements being 18 inches vertically and 14 inches horizontally (fig. 1A). This had been present since birth.

It was interesting to note that this man had been with the forces in North Africa and Italy but on no single occasion had he exposed his back in the company of his friends such as in shower baths, sea bathing in the Mediterranean or sun bathing. He was intensely shy and introspective and would hardly submit to a medical examination.

The patient was physically well. The affected area on the back was covered by a black, hairy nevus, raised in parts into verrucous and horny elevations.

*First Operation.*—On Feb. 16, 1944, about half the nevus was excised. In spite of good and quick hemostasis and the use of a drip blood transfusion, the anesthetist reported that the patient would not stand removal of the whole area.

*Second Operation.*—On February 24, strips of Thiersch graft were applied on the granulating area.

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From the Department of Surgery, University of Pretoria.

1. Pickrell, K. L., and Clay, R. C.: Giant Nevus of the Thigh Successfully Treated by Complete Excision and Primary Grafting, *Arch. Surg.* 48:319-324 (April) 1944.

*Third Operation.*—On March 24 the rest of the nevus was removed and strip Thiersch grafts were applied to the remaining raw area.

Healing occurred rapidly, and this was followed by a course of oil massage.

About one-half inch (1.27 cm.) of normal skin was removed beyond the edge of the nevus, leaving a raw area of over 280 square inches (1,692 sq. cm.) to cover.

The patient was seen in June 1945, when a photograph (fig. 1B) showed complete healing, the area being covered by soft, pliable skin, now freely movable over the underlying deep fascia. He was a changed man psychologically.

A letter from him dated May 7, 1948, states that he is perfectly well, that his back has not troubled him at all, that he has married and that he has a bonny daughter, who does not have a "birthmark."



A, enormous nevus, present since birth; B, complete healing after excision and skin grafting.

#### SUMMARY

A giant nevus, measuring 18 by 14 inches (45 by 35 cm.) is described. The nevus was totally excised and the defect covered by Thiersch grafts.

Until relatively recently giant nevi have been considered medical curiosities, but it is advocated that these lesions should be excised and the defect grafted, in a single stage procedure as in the case of Pickrell and Clay<sup>1</sup> or in a multiple stage procedure as in the case described here.

I would suggest that the multiple stage procedure with strip Thiersch grafts be employed, as a large raw area can be covered with a relatively small piece of skin. Removal of numerous drums of skin from the body with a dermatome is liable to leave marked visible discolorations.

# ROLE OF THE TRANSVERSE ABDOMINAL INCISION AND EARLY AMBULATION IN THE REDUCTION OF POSTOPERATIVE COMPLICATIONS

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AND

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THE PROBLEM of how best to approach the peritoneal cavity with a minimum of postoperative complications has challenged the attention and acumen of surgeons for many years. One may consult the references given in this paper for a review of the work of the many who have contributed to this problem of the proper abdominal incision<sup>1</sup> and the concepts of early ambulation.<sup>2</sup>

The purpose of this paper is to review briefly the fundamental anatomic and physiologic principles and to tabulate the clinical results which have led us to use routinely the transverse abdominal incision as well as to emphasize early ambulation increasingly.

Langer's lines of skin cleavage are situated transversely; hence, an incision which parallels them will close with less tension and leave a finer scar when it heals.

The oblique muscles originate laterally and, becoming aponeurotic, pass in an essentially transverse direction to insert into the linea alba, having formed the anterior and posterior rectus sheaths.<sup>3</sup> The external and internal oblique muscles practically never vary more than 30 degrees from the transverse plane,<sup>1</sup> while the transversus abdominis is truly transverse. If the aponeurotic fibers are visualized as multiple small tendons,<sup>4</sup> it is apparent that a vertical incision divides them at right angles to their courses while a transverse incision tends to

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From the Department of Surgery, University of Michigan Medical School.

1. Rees, V. L., and Coller, F. A.: Anatomic and Clinical Study of the Transverse Abdominal Incision, *Arch. Surg.* **47**:136-146 (Aug.) 1943.

2. Leithauser, D. J.: Confinement to Bed for Only Twenty-Four Hours After Operation, *Arch. Surg.* **47**:203-215 (Aug.) 1943.

3. McVay, C. B., and Anson, B. J.: The Composition of the Rectus Sheath, *Anat. Rec.* **77**:213-225 (June 25) 1940.

4. Moschowitz, A. V.: Transverse Incisions in the Upper Abdomen, *Ann. Surg.* **64**:268-287 (Sept.) 1916.

parallel their courses. Incision of the aponeuroses transversely is less traumatizing and therefore the more sound procedure physiologically. The intact fibers adjacent to the transverse incision provide firmer anchorage for suture material than do the cut ends of fibers presenting at the margins of the vertical incision.

The rectus abdominis passes vertically from the pubes to the xiphoid process and the adjacent ribs. The muscle is narrow below and broad above, occasionally approaching the anterior axillary line laterally.<sup>1</sup> Three equally spaced tendinous inscriptions firmly attach the muscle to the anterior rectus sheath, above the level of the umbilicus. Occasionally four or more are present, and the additional ones are equally spaced below the umbilicus. These inscriptions allow minimal retraction of the transected muscle, making for accurate approximation with simple suture of the sheaths. Below the umbilicus firm healing follows suture of the anterior sheath, as demonstrated repeatedly at reoperation.

The oblique muscles provide protection and play a major role in altering intra-abdominal pressure, so closely related to respiration and therefore of prime concern postoperatively.

The lower six intercostal and first lumbar nerves supply the abdominal wall (fig. 1). All pass in an essentially transverse direction, anastomose richly in the wall and terminate in the recti, where anastomoses are deficient.<sup>1</sup> The transverse incision tends to parallel their courses and provides opportunity for their visualization, thereby reducing traumatization. The vertical incision is prone to sever or contuse them, giving rise to pain and splinting as a result of hyperirritability. Painful scars due to neuromas<sup>5</sup> and atrophy of the muscle segments involved are possible late results of such trauma.

The blood supply of the abdominal wall is derived largely from the superior and inferior epigastric vessels. The vertical incision is parallel to them and thus spares them, while the transverse incision in the upper and lower quadrants cuts across them. Anastomoses are rich enough, however, to assure tissue viability.

Since the oblique muscles with their aponeuroses hold the major role, in so far as the anterior abdominal wall is concerned, in altering intra-abdominal pressure, they become an integral part of the respiratory mechanism. Deep breathing and coughing,<sup>6</sup> essential in the prevention and treatment of postoperative pulmonary complications, are facilitated by the strong contracture of these muscles. Interference with this action jeopardizes the efficient performance of these respiratory acts. The resultant of forces on contracture of the oblique muscles is in the trans-

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5. Bancroft, F. W.: Painful Postoperative Abdominal Scars, *Arch. Surg.* **21**:289-299 (Aug.) 1930.

6. Haight, C., and Ransom, H. K.: Observations on the Prevention of Atelectasis and Bronchopneumonia, *Ann. Surg.* **114**:243-262 (Aug.) 1941.

verse plane; hence, it is true that the vertical incision will have greater stress placed on it during the respiratory cycle than will the transverse. Sloan<sup>7</sup> emphasized this by measuring, in 20 different patients, the force needed to approximate the edges of an L-shaped incision while the patient was under light general anesthesia. In every case he found that the force required to approximate the vertical limb was about thirty times greater than that necessary to approximate the transverse limb.

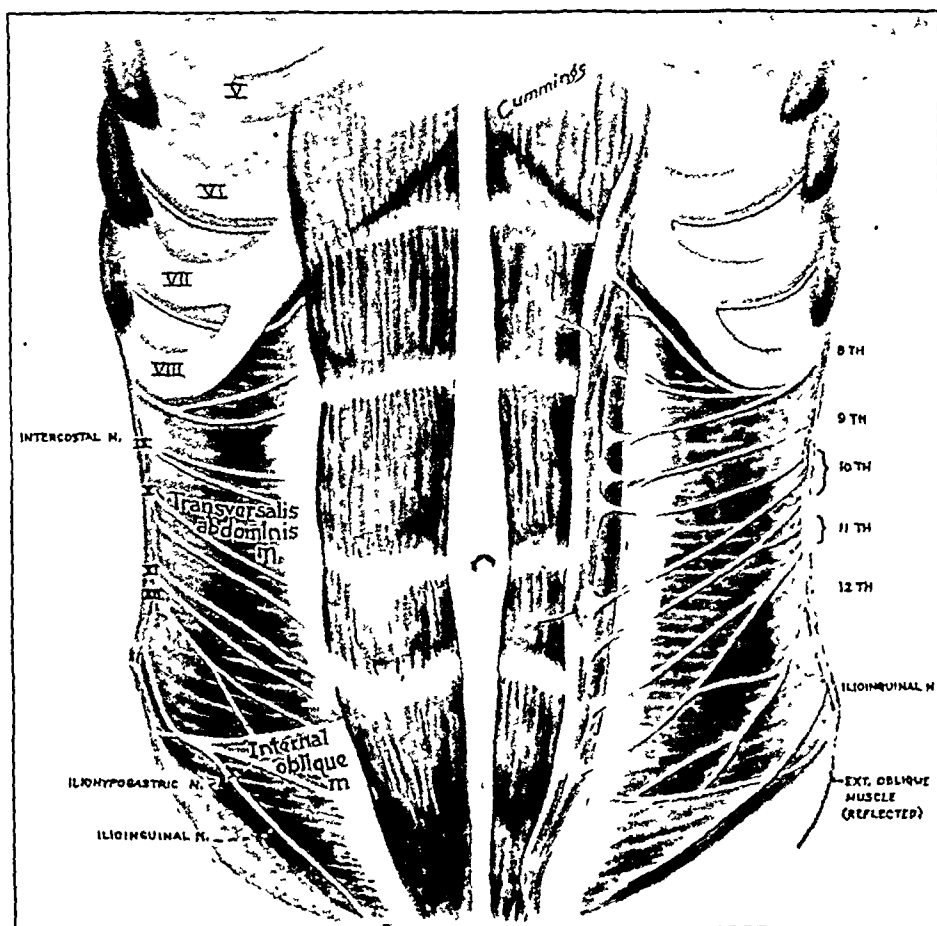


Fig. 1.—The courses of the intercostal nerves and their anastomoses. The tendinous inscriptions, which attach the rectus muscle to its anterior sheath, are shown. (From Rees, V. L., and Coller, F. A.: *Arch. Surg.* 47:136-146 [Aug.] 1943.)

One of the consequences of this increased stress is less efficient respiration with reduction in vital capacity, which may be as much as 58 per cent below normal, according to Beecher.<sup>8</sup> With these facts in

7. Sloan, G. A.: A New Upper Abdominal Incision, *Surg., Gynec. & Obst.* 45:678-687 (Nov.) 1927.

8. Beecher, H. K.: The Measured Effect of Laparotomy on the Respiration, *J. Clin. Investigation* 12:639-650 (July) 1933.



mind one may state that the transverse incision will give rise to far less interference with the respiratory mechanism than will the vertical incision.

The peritoneum, being closely adherent to the transversalis fascia and thus to the posterior rectus sheath (above the umbilicus), is subjected to the stresses of those structures, as all usually are closed in one layer. As the vertical incision is subjected to far greater stress than is the transverse incision, so will it be reflected in the peritoneal suture line, with consequent greater pain, resulting in splinting and diminished respiratory excursion. Separation of the peritoneal suture line preceded by that in the transversalis fascia or posterior rectus sheath or both provides a nidus for wound disruption, adherence of bowel or, later on, adhesions. Incisional hernia may have its start in such a process.

Pain is minimal in the patient with the transverse incision because tension on the skin is lessened, nerves are preserved and the aponeurotic, fascial and peritoneal suture lines are under less stress. Therefore, deep breathing, coughing, moving about in bed, bed exercises and early ambulation are facilitated.

The transverse incision provides excellent exposure in the upper, middle or lower quadrants and is used exclusively for all abdominal operations at this hospital. All incisions are fashioned in a similar manner. Each layer from the skin through the peritoneum is incised in the transverse plane. Patients having a narrow costal angle and undergoing total gastrectomy or vagotomy frequently require a short vertical extension of the upper abdominal, transverse incision. The rectus muscle is partially or totally divided, or as in gastrectomy, both recti are transected. The oblique muscles are split in the direction of their fibers. Closure is accomplished by means of a double strand of 000 chromic surgical gut used as a running stitch in the peritoneum and the posterior rectus sheath, below the umbilicus in the peritoneum and transversalis fascia. Recently one of us (F. A. C.) has been using interrupted, fine, stainless steel wire sutures for this layer. The aponeuroses and anterior rectus sheaths are closed with interrupted silk or wire sutures. During the latter half of the period covered by this study the layers were closed almost exclusively with stainless steel wire, size 32. The subcutaneous tissue is closed with a running strand of wire singly or in tiers, depending on the thickness of the panniculus. The skin is closed by means of a continuous subcuticular strand of wire (fig. 2). The cutaneous and subcutaneous sutures are removed on the seventh postoperative day. No suture material remains in the subcutaneous tissue, and there are no sutures placed in the rectus muscle. Silk was substituted for wire in the skin and subcutaneous tissue in about 30 per cent of the cases covered by this study. No retention sutures of any type are used.

Wire is the suture material of choice for abdominal wounds, not because of its strength but because it incites measurably less inflammatory reaction than any other material. This fact has been proved by experimentation on animals and has been observed clinically. Fine silk is used for ligatures.

In cases of contamination, such as peritoneal soiling during an anastomosis or an abscess adjacent to a slowly perforating carcinoma, the delayed primary closure technic is carried out. This closure is exactly like that previously described up to the subcutaneous layer.

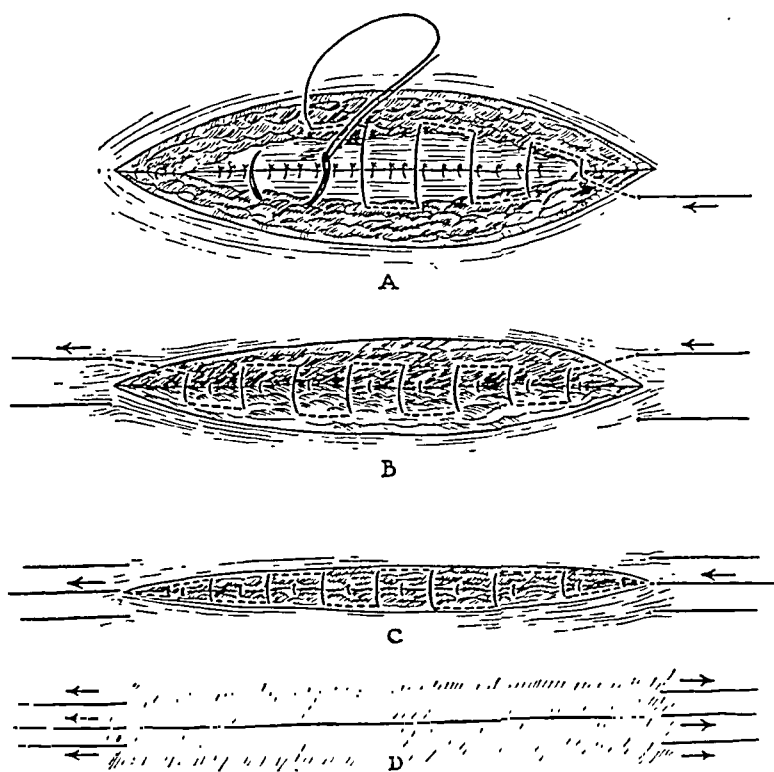


Fig. 2.—Our method of closing the subcutaneous tissue and skin with stainless steel wire. *A*, the first layer is subcutaneous fat. *B*, when necessary a second suture is made in the same layer. *C*, subcuticular wire suture. All sutures in these layers are removed on the seventh postoperative day, leaving no foreign material in the skin or subcutaneous tissue.

The skin and the subcutaneous tissue are not approximated; however, figure-of-8 silk sutures are placed. A suitable loose pack holds the skin edges apart for forty-eight hours, at which time the wound is inspected, and if uninfected it is closed by tying the previously placed silk sutures.

The vertical incisions used were of the standard type, and closure was obtained by the use of fine, chromic surgical gut for the peritoneum-posterior rectus sheath layer and wire or silk for the aponeuroses and for the skin.

In order to determine the results of the use of the transverse incision and early ambulation as compared to the vertical incision and late ambulation, 1,363 consecutive operative cases were reviewed. The numerical details concerning type of incision and ambulation are shown in the tables.

All operative procedures were intraperitoneal and all were major, herniorrhaphy or appendectomy not being included. The operations were carried out by various members of the general surgical staff of the University Hospital. Factors other than type of incision and time of ambulation were as nearly similar as it is possible for them to be.

There were 616 (45 per cent) patients who had malignant disease of the gastrointestinal tract. Eight hundred and eighty (65 per cent) of the operative procedures were on the stomach or the large or small bowel, and the vast majority were resections of some type. Four hundred and forty-four operations (32 per cent) were on the biliary system, 161 including an attack on the common duct. The patients were, as one would expect in a group 45 per cent of whom had a malignant condition, over 50 years of age, with many past 60. No case in which drainage of infection was the primary indication for operation was included. All wounds were closed primarily or by the technic of delayed primary closure.

The data tabulated for each case are as follows: (1) number of postoperative days in the hospital, (2) pulmonary complications, (3) vascular complications, (4) wound infections, (5) wound disruption, (6) postoperative obstruction and (7) incisional hernia.

Table 1 shows the average postoperative stay in the hospital. This table is set up exactly as those to follow and needs some explanation. The T column indicates transverse incision, with early and late ambulation included. Columns E. A. and L. A. denote early and late ambulation with both types of incisions included under each. Column T. E. A. includes those patients having a transverse incision in whom ambulation was carried out early, while column V. E. A. indicates early ambulation for those patients with a vertical incision. The last two columns (T. L. A. and V. L. A.) compare transverse and vertical incisions, ambulation having been carried out late in all the patients. The bottom row of figures indicates the total number of cases included in each category; thus, in 523 patients a transverse incision and early ambulation were employed, while in 412 vertical incisions were used and ambulation was carried out late.

Early ambulation, so far as this report is concerned, means that the patient is out of bed and moving about periodically and progressively from the first twenty-four postoperative hours.

Table 1 demonstrates that the use of transverse incision plus early ambulation results in the shortest postoperative stay in the hospital,

sixteen days. The use of the vertical incision with late ambulation results in the longest stay, twenty-three days.

Table 2 gives the number and percentage of pulmonary complications for each category. The pulmonary complications included infarcts, patchy or massive atelectasis and pneumonia. All diagnoses were made clinically and confirmed roentgenologically and/or bronchoscopically. Transverse incision plus early ambulation gave the lowest rate of pulmonary complications, while vertical incision plus late ambulation gave the highest, 3 per cent and 11 per cent, respectively. Vertical incision with early ambulation, although used in a comparatively small group (191 cases), gave 7 per cent pulmonary complications, as compared with 3 per cent for transverse incision with early ambulation. Transverse incisions plus

TABLE 1.—*Postoperative Stay in the Hospital*

	T *	V	E.A.	L.A.	T.E.A.	V.E.A.	T.L.A.	V.L.A.
Postoperative hospital days.....	17	20	17	20	16	17	17	23
Total cases.....	760	603	714	649	523	191	237	412

\* T indicates transverse incision; V, vertical incision; E.A., early ambulation; L.A., late ambulation; T.E.A., transverse incision with early ambulation; V.E.A., vertical incision with early ambulation; T.L.A., transverse incision with late ambulation, and V.L.A., vertical incision with late ambulation.

TABLE 2.—*Pulmonary Complications*

	T	V	E.A.	L.A.	T.E.A.	V.E.A.	T.L.A.	V.L.A.
Pulmonary complications.....	29 4%	57 10%	27 4%	59 9%	13 3%	14 7%	16 7%	43 11%
Total cases.....	760	603	714	649	523	191	237	412

early and late ambulation were compared with transverse incisions plus early ambulation, and the former gave 4 per cent pulmonary complications as compared with 3 per cent for the latter. Transverse and vertical incisions were compared and the former has 4 per cent pulmonary complications as compared with 10 per cent for the latter. A similar comparison between early and late ambulation shows 4 per cent for the former and 9 per cent for the latter.

Table 3 depicts the results for vascular complications. The complications considered were phlebothrombosis and thrombophlebitis. Diagnoses were made clinically and in most cases confirmed by observing the clot at the time of venous ligation. There is little of statistical significance here except for the comparison between columns T. E. A. and V. E. A., indicating a 2 per cent difference in favor of the transverse incision in the rate of vascular complications when ambulation was a constant factor.

Table 4 is a record of the rate of wound infection. The rate of infection is high. That the infections were mild is indicated by the fact that the average postoperative stay in the hospital was increased only three to four days. One should recall also that we are dealing here with an elderly group whose general nutrition is not of the best (45 per cent of the 1,363 patients had malignant disease of the gastrointestinal tract). The procedures were all of considerable magnitude and were, in the main, carried out by the resident staff, both factors tending to make the operating time fairly lengthy. The transverse incision has a rate of wound infection of 3 per cent, as compared to 6 per cent for the vertical

TABLE 3.—*Vascular Complications*

	T	V	E.A.	L.A.	T.E.A.	V.E.A.	T.L.A.	V.L.A.
Vascular complications.....	14 2%	18 3%	17 2%	15 2%	10 2%	7 4%	4 2%	11 3%
Total cases.....	760	603	714	649	523	191	237	412

TABLE 4.—*Incidence of Wound Infection*

	T	V	E.A.	L.A.	T.E.A.	V.E.A.	T.L.A.	V.L.A.
Wound infections....	19 3%	33 6%	25 4%	27 4%	14 3%	11 6%	5 2%	22 6%
Total cases.....	760	603	714	649	523	191	237	412

TABLE 5.—*Incidence of Wound Disruption*

	T	V	E.A.	L.A.	T.E.A.	V.E.A.	T.L.A.	V.L.A.
Wound disruption...	4 0.5%	14 2.5%	10 1.5%	8 1.0%	3 0.5%	7 3.5%	1 0.4%	7 1.5%
Total cases.....	760	603	714	649	523	191	237	412

incision. Ambulation plays no part here as shown by comparing columns E. A. with L. A., T. E. A. with T. L. A. and V. E. A. with V. L. A.

Table 5 shows the rate of wound disruption. The rate of evisceration is appreciably increased when early ambulation is carried out by the patient who has a vertical incision. (Compare columns V. E. A. and V. L. A.) The rate of disruption varies only slightly when the transverse incision is used, whether ambulation is carried out early or late. (Compare columns T. E. A. and T. L. A.) Seventy-five per cent of the eviscerations of transverse incisions occurred in infected wounds, while 64 per cent of the disruptions of vertical incisions occurred in infected wounds. These figures indicate that more clean vertical wounds disrupt than is the case with clean transverse wounds and that infection is a large factor in disruption of incisions.

Table 6 deals with postoperative obstruction. Mechanical obstruction occurring during the early postoperative period is considered. In each case operation was required to relieve the obstruction, and only obstructions which resulted from incisional defects are included. The complication is infrequent in this group, being present nine times, an incidence of 0.7 per cent in 1,363 cases. The figures reveal that the patients with transverse incisions for whom ambulation was carried out early have a lower incidence of mechanical obstruction except for those for whom vertical incision plus early ambulation was used, and that is a comparatively small group. (Compare column T with V, E. A. with L. A. and T. E. A. with V. L. A.)

In the consideration of incisional hernia a follow-up report covering at least eighteen postoperative months was required. Three hundred and

TABLE 6.—*Postoperative Obstruction*

	T	V	E.A.	L.A.	T.E.A.	V.E.A.	T.L.A.	V.L.A.
Postoperative obstruction.....	2 0.3%	7 1.3%	2 0.3%	7 1.0%	2 0.5%	0 ..	0 ..	7 1.5%
Total cases.....	760	603	714	649	523	191	237	412

TABLE 7.—*Incidence of Incisional Hernia*

	T	V	E.A.	L.A.	T.E.A.	V.E.A.	T.L.A.	V.L.A.
Incisional hernia.....	7 1.3%	16 3.2%	7 1.3%	16 3.1%	4 1.0%	3 1.9%	3 1.7%	13 4%
Total cases.....	552	499	537	514	374	155	178	344

twelve cases were excluded because of inadequate follow-up. When examining the figures in table 7 one must recall that we are dealing with an elderly group in which there was a high incidence (45 per cent) of malignant disease. The lowest incidence of incisional hernia occurred in patients for whom the transverse incision combined with early ambulation was used (1 per cent). The highest incidence was in those for whom the vertical incision plus late ambulation was employed (4 per cent). Infection had been present in about one half of the incisions in which hernia later developed, this being true for both the transverse (3 of 7 hernias) and the vertical incisions (7 of 16 hernias).

## COMMENT

In an attempt to determine the relative importance of the transverse incision and early ambulation in the reduction of postoperative complications the foregoing tables were made for comparison. A perusal of table 1 seems to point to the fact that the type of incision and the time of ambulation play about an equal role in reducing the postoperative

days in the hospital, the shortest average stay being recorded for the transverse incision combined with early ambulation.

Pulmonary complications, as the statistics show (table 2), are influenced about equally by early ambulation and the transverse incision. It is felt that the transverse incision with wire suture material makes the patient more comfortable and therefore early ambulation is carried out more willingly and more efficiently. Patients who cannot be ambulatory until late in the forty-eight hour period or later are able to breathe deeply, cough and carry out bed exercises with a facility not observed in patients in whom a vertical incision has been made.

Vascular complications are influenced somewhat more by the transverse incision than by early ambulation, as shown in table 3. This is a reflection of the same factors as those mentioned before concerning reduction of pulmonary complications.

The incidence of wound infection is lower when the transverse incision is used than when the vertical incision is used, ambulation having practically no influence (table 4). Devitalization of tissue due to increased tension required to close the vertical wound is a possible explanation for the higher rate of infection.

The value of the transverse incision is well illustrated in the consideration of evisceration. Wound disruption is more frequent in patients who are ambulatory early (table 5). When the vertical incision is used, early ambulation results in an incidence of disruption of 3.5 per cent. When the transverse incision is employed the incidence with early ambulation is 0.5 per cent.

The generally improved tonus of the patient who is ambulatory early would tend to decrease the over-all incidence of postoperative obstruction. Factors which cause mechanical obstruction have less opportunity to become prominent when the transverse incision is used instead of the vertical one, as borne out by the reduced incidence of that complication with the use of the former (table 6).

The transverse incision is responsible for the reduction in the incidence of incisional hernia. This has been a common observation in any comparison between the two incisions and is a reflection of the anatomic and physiologic factors discussed earlier.

Two objections to the transverse incision often mentioned are consumption of time and lack of ease of extension up or down. It is true that the transverse incision does take somewhat longer to fashion, but frequently this time is made up because of ease of closure of this incision as compared to the vertical one. Lightening of the anesthesia, with consequent tightening of the abdominal musculature, does not interfere with the closure of the transverse wound to the degree noted with the vertical incision. Modern methods of diagnosis infrequently leave doubt as to the location of the pathologic process, and therefore the

location of the incision can be decided on with the assurance that in only a small number of cases will revision be necessary. It is generally better to close the original transverse incision and make a new one than to attempt revision of the original incision.

We have observed no complication which could be attributed to transection of one or both rectus muscles.

#### CONCLUSIONS

1. The transverse incision is the most sound surgical approach physiologically to the peritoneal cavity.

2. Deep breathing, coughing, moving about in bed and bed exercises are carried out with less discomfort and more efficiency by patients in whom the transverse incision has been used.

3. Early ambulation is accomplished with more abandon and less discomfort and is accompanied with a far lower incidence of wound disruption when the transverse incision is used instead of the vertical one.

4. The transverse abdominal incision used in combination with early ambulation lowers the incidence of all postoperative complications studied in this series of cases and results, therefore, in a reduction in the number of postoperative days in the hospital.



# MANAGEMENT OF CANCER OF THE LOWER PART OF THE BOWEL

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THE IMPORTANCE of cancer of the lower part of the bowel cannot be overemphasized when one considers that it still remains the fourth most common malignant process involving the human organism; of those of the gastrointestinal tract, it is second in frequency to cancer of the stomach. In this discussion it is our purpose to consider the preparation of the patient, choice of operative procedure and post-operative treatment, with particular reference paid to the technic of abdominoperineal proctosigmoidectomy without colostomy and preservation of the sphincter musculature.

Advances in management of cancer of the lower part of the bowel have diminished markedly the mortality rate accompanying operative procedures undertaken for this disease. This is well demonstrated in our own series of cases, which includes 640 patients with malignant growths of the anus, rectum and sigmoid colon, shown in table 1.

## PREOPERATIVE EVALUATION AND PREPARATION

In order to prepare patients with any degree of adequacy for a major operation on the colon and rectum, it is essential that they be hospitalized for a period of several days. During this time, an effort is made to evaluate the patient as a surgical risk and, in so far as it is possible, ensure the optimal nutritional, fluid, electrolyte, nitrogenous and vitamin balance. The studies enumerated in the outline have been of definite value in the evaluation of our patients preoperatively.

The presence of hepatic dysfunction was noted by Abels<sup>1</sup> in 25 per cent of patients with malignant growths of the gastrointestinal tract. On a small scale, similar studies were undertaken in our department,

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Read before the Sectional Meeting of the Nebraska Chapter of the International College of Surgeons, Lincoln, Neb., May 22, 1947.

1. Abels, J. C.; Rebers, P. E.; Binkley, G. E.; Pack, G. F., and Rhoads, C. P.: Metabolic Studies in Patients with Cancer of the Gastrointestinal Tract: II. Hepatic Dysfunction, *Am. J. Med.* **16**:221, 1942.

*Studies for Evaluating Patients Preoperatively*

## Routine

1. Complete blood count, hemoglobin and hematocrit value
2. Daily specific gravity of urine
3. 2,500 to 3,500 cc. intake
4. Serum protein with albumin-globulin ratio
5. Blood urea, fasting blood sugar
6. Weight in kilograms (daily)
7. Daily fluid intake and output
8. Medical and urologic consultation (including electrocardiographic and cystometric studies)
9. Blood type and Rh factor
10. Daily blood pressure
11. Photofluorogram of chest

## Elective

1. Liver Function
  - (a) Sulfobromophthalein
  - (b) Cephalin flocculation
  - (c) Thymol turbidity
  - (d) Prothrombin time
  - (e) Alkaline serum phosphatase
2. In cases of obstruction, ulcerative colitis or dehydration
  - (a) Carbon dioxide content (or blood  $p_H$ )
  - (b) Blood chlorides
  - (c) Blood sodium and potassium
3. Barium enema (in absence of obstruction) to demonstrate presence of other lesions

but confirmation of such definite evidence of dysfunction was not demonstrable. It was interesting to note that, contrary to previous reports,<sup>2</sup> the alkaline serum phosphatase reaction was normal in 10 patients

TABLE 1.—*Cancer of the Anus, Rectum and Sigmoid*

Number of patients.....	640			
Number operated on.....	579			
Operability rate.....		90.4%		
Number in whom resection was done.....	514			
Resectability rate.....		80.3%		
			Cases	Deaths
				Per-
				cent-
				age
Abdominoperineal proctosigmoidectomy.....	After Babcock	344	17	4.9
Abdominoperineal excision—one stage.....	Miles	67	3	4.4
Abdominoperineal excision—two stage.....	Lahey	6	1	16.6
Sigmoidectomy—multiple stage.....	Mikulicz-Rankin	32	3	9.3
Sigmoidectomy—single stage.....	Open or closed	28	2	7.1
Perineal excision with colostomy.....	Lockhart-Mummery	22	1	4.5
Anterior resection.....	Hartmann	11	0	0
Perineoabdominal resection.....	Gabriel-Turner	2	0	0
Perineal excision.....	Cuneo-Seneque	2	0	0
Total.....		514	27	5.2

with massive metastasis to the liver. Occasionally, definite evidence of hepatic dysfunction has been demonstrated by the sulfobromophthalein or cephalin flocculation test. This almost invariably occurs in patients who are anemic, hypoproteinemic, malnourished and clinically poor risks. Consequently, for this group of patients varied liver function tests are ordered. When evidence of dysfunction exists, the operation is delayed until an attempt has been made to remedy the condition.

Anemia and hypoproteinemia, when present, are corrected immediately with whole blood, plasma and a high protein intake in order to provide an erythrocyte count of 4,500,000 with a concomitant hemoglobin value of 80 to 90 per cent, hematocrit readings of 40 or above and normal serum protein values. Determination of the  $p_H$  factor is routine.

2. Bullard, R. W.: Alkaline Phosphates and Metastatic Liver Disease, *Surgery* 19:379, 1946.

The skin is prepared for three days preoperatively. A new substance, "G-11," used experimentally by Seastone,<sup>3</sup> holds promise as an effective agent for preoperative preparation of the abdominal skin. A fluid intake of 2,500 to 3,000 cc. is maintained. In order to prevent shock and maintain a positive nitrogen balance with greater ease postoperatively, 1,000 cc. of blood is made available for each abdominoperineal resection. One will recall the recent investigations of Pack<sup>4</sup> and Collier<sup>5</sup> demonstrating the loss of blood as varying from 250 to 900 cc. during this procedure.

#### NUTRITION

The presence of avitaminosis and malnutrition, particularly hypoproteinemia, has been demonstrated consistently in patients with malignant growths of the gastrointestinal tract.<sup>6</sup> It is necessary, therefore, to furnish these patients with a well balanced, high protein, high caloric, high vitamin diet which yields no residue but contains adequate amounts of both minerals and vitamins.

#### PROTEIN NUTRITION

Research along nutritional lines has largely been devoted to the study of protein metabolism.<sup>7</sup> As a result, it is now an established fact

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3. Seastone, C. V.: Observations on the Use of G-11 in the Surgical Scrub. *Surg., Gynec. & Obst.* **84**:355, 1947.

4. Pack, G. E.; Oppenheim, A.; Abels, J. C., and Rhoads, C. P.: Estimation and Significance of Blood Loss During Gastrointestinal Surgery, *A. J. Surg.* **119**: 871, 1944.

5. Collier, F. A., and Crook, C. E.: Blood Loss in Surgical Operations, *J. A. M. A.* **126**:1 (Sept. 2) 1944.

6. Binkley, G. E.; Abels, J. C., and Rhoads, C. P.: The Treatment of Post-operative Hypoproteinemia in Patients with Cancer of the Colon and Rectum, *Ann. Surg.* **118**:366, 1943. Abels, J. C.; Rebers, P. E.; Pack, G. E., and Rhoads, C. P.: Metabolic Studies in Patients with Cancer of the Gastrointestinal Tract, *Ann. Surg.* **118**:366, 1943. Meyer, K. A., and Kozoll, D. D.: Protein Deficiency in Surgical Patients, *Surg., Gynec. & Obst.* **78**:181, 1944. Bacon, H. E.; Todhunter, W. D.; Gass, O., and Wolfe, F. D.: The Preoperative and Postoperative Treatment of Cancer of the Rectum and Pelvic Colon, *J. Internat. Coll. Surgeons* **8**:20, 1945.

7. Elmen, R., and Lischer, C.: The Occurrence and Correction of Hypoproteinemia in Surgical Patients, *Surg., Gynec. & Obst.* **76**:503, 1943. Mulholland, J. H.; Co Tui, F.; Wright, A. M.; Vinci, V. G., and Shafiroff, B.: Protein Metabolism and Bedsores, *Ann. Surg.* **118**:1015, 1943. Thompson, W. D.; Raydin, I. S., and Frank, J. L.: Effect of Hypoproteinemia on Wound Disruption, *Arch. Surg.* **36**:500 (March) 1938. Rhoads, C. P.; Fliegelman, W. I., and Panzer, L. M.: Mechanism of Delayed Wound Healing, *J. A. M. A.* **118**:21 (Jan. 3) 1942. Jones, C. M.: Protein Deficiency, *New England J. Med.* **215**:1152, 1936. Best, C. H., and Taylor, W. A.: *Physiological Basis of Medical Practice*, Baltimore, Williams & Wilkins Company, 1945. Elman, R.: The Practical Use of Amino Acids in Protein Nutrition, *J. A. M. A.* **128**:659 (June 30) 1945.

that body proteins are depleted and protein metabolism is disturbed by disease processes. The frequency with which hypoproteinemia occurs in patients with malignant tumors of the gastrointestinal tract has been mentioned previously. Attention has been called to the important role that hypoproteinemia plays in wound healing, predisposition to shock, postoperative edema in wounds and surrounding suture lines, increased susceptibility to infection, anesthesia and hepatic dysfunction. Casual mention is made of these points with the sole idea of stressing the importance of correcting protein depletion and establishing large reserves of protein preoperatively as well as the maintenance of a positive nitrogen balance postoperatively.

#### PREPARATION OF THE BOWEL

Careful preparation of the bowel prior to surgical intervention has undoubtedly served as a tremendous factor in lowering the mortality rate following resection of the colon and rectum. Phthalylsulfathiazole (sulfathalidine®) has been our preference, being used routinely in doses of 0.1 Gm. per kilogram of body weight, as recommended by Poth.

In some instances, when a moderate degree of obstruction is present, the substitution of succinylsulfathiazole (sulfsuxidine®) is advisable because of its laxative effect. In regard to the use of agents for lowering the bacterial flora of the colon, it might be interesting to relate that our department, in conjunction with Professor Earl Spaulding, head of the department of bacteriology, has been investigating the efficacy of streptomycin administered orally. Zintel and others<sup>8</sup> have recently reported good results with this same method in reducing the coliform organisms, *Streptococcus faecalis* and the clostridial group. Our results have been somewhat at variance with those reported by this group and are given elsewhere in detail.<sup>9</sup> However, it should be stated that streptomycin holds promise as an adjunct in the preparation of the bowel for operation. Comparative results of the use of phthalylsulfathiazole, streptomycin and a combination of the two are shown in the accompanying charts. It should be stated that reversion was observed, for which reason administration of streptomycin for only two days prior to operation is recommended. Large doses of cathartics are contraindicated since dehydration, with more than probable loss of proteins and

8. Zintel, H. A.; Wyle, M.; Nichols, A., and Rhoads, C. P.: The Use of Streptomycin in Surgical Patients, *Surgery* **21**:178, 1947.

9. Rowe, R. J.; Spaulding, E., and Bacon, H. E.: Evaluation of Oral Streptomycin as an Adjunct in Preparing the Bowel for Surgery, read before the American College of Surgeons, New York city, September 1947. Bacon, H. E., and Rowe, R. J.: Preparation and After-Care of the Patient Undergoing Surgery of the Lower Bowel, read before the Gastroenterologic section, A. M. A., Atlantic City, New Jersey, June, 1947.

valuable water-soluble vitamins, occurs. Rectal irrigation with sodium bicarbonate and phthalylsulfathiazole is carried out, with aspiration from six to eight hours prior to operation. Thereafter, the rectal tube is left in situ and is taped to the buttocks. A Foley catheter is routinely employed. Additionally, a Levin tube is passed into the stomach and continuous suction applied during the operation to prevent vomiting and aspiration of vomitus. It is our opinion that this procedure has

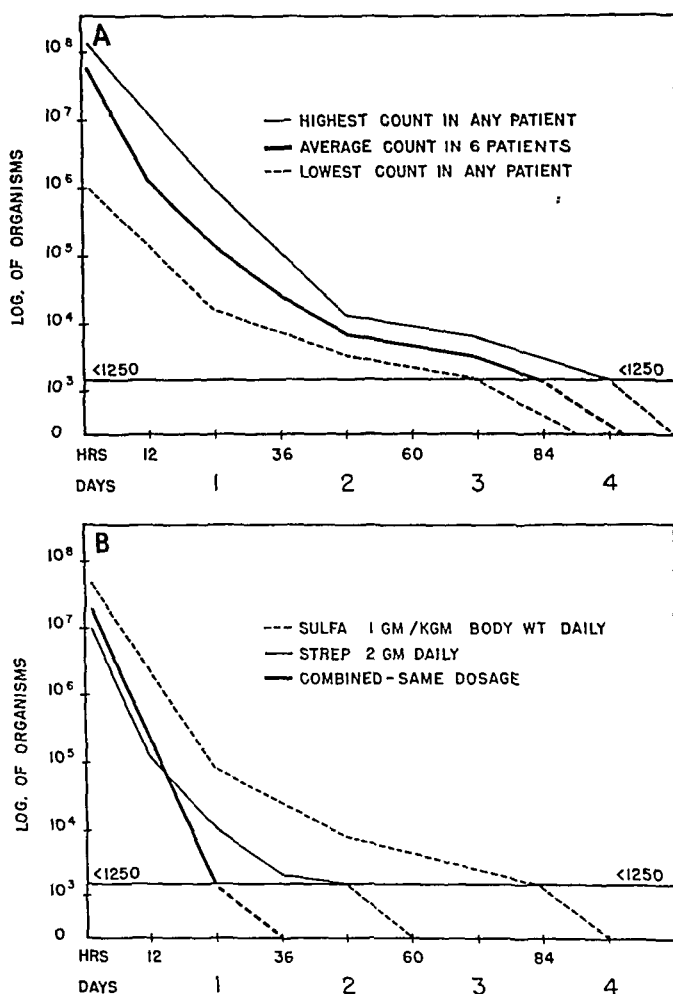


Fig. 1.—*A*, coliform counts during administration of phthalylsulfathiazole (sulfathalidine,<sup>®</sup> 0.1 Gm. per kilogram of body weight daily). *B*, average coliform counts.

definitely decreased the incidence of atelectasis. In impending obstruction, or as an adjunct to primary restriction, the mercury-weighted Miller-Abbott tube has proved useful. However, should definite evidence of obstruction be present, proximal enterostomy is preferable. In this group of patients, it is imperative to establish fluid and electrolyte balance prior to operative procedures.

## CHOICE OF OPERATIVE PROCEDURES

Operative procedures for the removal of cancerous growths must, of necessity, conform to several qualifications. As nearly as possible, the growth and its extension to adjacent organs and to blood and lymphatic vessels, must be completely extirpated by a procedure com-

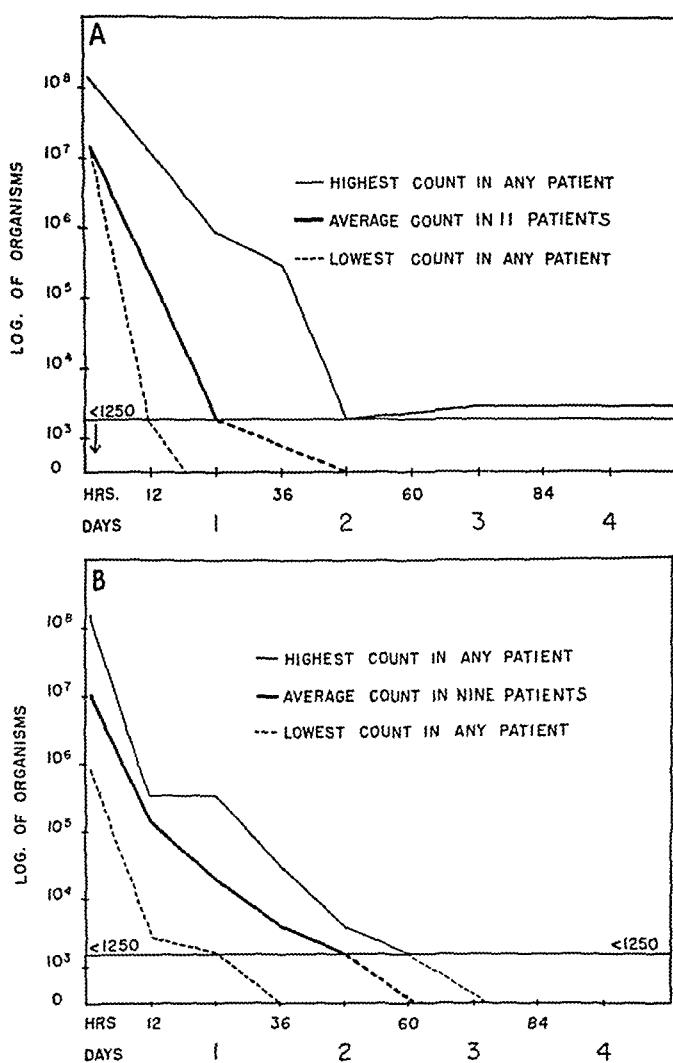


Fig. 2.—*A*, coliform counts with streptomycin (2 Gm. daily) and sulfathalidine® (0.1 Gm. per kilogram of body weight daily) combined. *B*, coliform counts with streptomycin (2 Gm. daily).

patible with life and the probability of longevity. Concomitantly, it should restore function that approaches the normal. It is our opinion that abdominoperineal proctosigmoidectomy is a procedure adequately meeting these qualifications in a large majority of cases in which there are cancerous lesions of the lower part of the bowel. Yet we do not believe that the procedure is applicable to every case. Prior to the

enumeration of the indications for proctosigmoidectomy or the delineation of the areas to which it must be restricted, it might be in order to discuss the incidence of cancer in the lower part of the bowel, lymphatic spread and the blood supply to that area. In an effort to determine the precise location of the lesion in the bowel, records of 180 consecutive patients were studied, and the following data were obtained:

Location of Lesion	Patients
Sigmoid .....	23
Rectosigmoid .....	53—33.8%
	80.3%
Rectum (excluding lower 3 cm.) .....	73—46.5%
Anal canal (including lower 3 cm. of rectum) ..	31—19.7%
Total .....	<u>180</u>

On the assumption that lesions in the sigmoid are resected solely by an abdominal approach and those located in the lowest 3 cm. of the rectum and anal canal by a method necessitating removal of the sphincters, there remain 80.3 per cent in which the sphincters may be preserved, if the findings in recent histopathologic investigations merit acceptance.

All recent studies relevant to the lymphatic spread of carcinoma of the lower part of the bowel, including those of Westhues, Collier, Gilchrist, Dukes and Bussey and Waugh and Grover, tend to show that malignant growths located in this region do not spread distally. In our group of 146 cases in which the removed specimens of bowel were sectioned serially at 2, 4 and 6 cm. caudad to the growth, invasion was observed in but 1 instance at the 6 cm. level. As a result of these findings, we have been led to conclude that the sphincter musculature may be preserved, providing the lower margin of the malignant growth is at least 6 cm. from the anal margin.

It is evident from the questions received concerning proctosigmoidectomy that relatively few understand the technic of the procedure. This has led to the assumption that unfamiliarity with it is mainly due to the fact that a misconception exists of the blood supply to the distal part of the colon, the mobility of the bowel and the amount of bowel that may be extirpated by this method.<sup>10</sup> Briefly, the blood supply to this area of bowel is derived from the inferior mesenteric vessel, through the left colic, the sigmoidal and the superior hemorrhoidal vessels. The sigmoidal vessels vary in number from one to seven and, contrary to some reports, form a well developed arcade with the left colic vessel. After interruption of the inferior mesenteric vessel just below the left colic, there still remains adequate blood flow to nourish the sigmoid colon.

10. Bacon, H. E., and Smith, C. H.: Blood Supply of the Colon and Rectum, *Ann. Surg.* **127**:1 (Jan.) 1948.

From results attained by us in terms of five year survival, proctosigmoidectomy does not at all comprise radicability. Based on the method suggested by Newman, of the British Ministry of Health, the following fraction is employed:

$$\frac{\text{Alive at 5 years} \times 100}{\text{Resection deaths, less the number of those who are untraced or who died of other causes}}$$

Thus, our incidence of five year cures based on 76 patients on whom abdominoperineal proctosigmoidectomy was performed five or more years ago is 52.6 per cent. In this group of 76 patients, there were 20 cases conforming to grade "A" classification, as shown in table 2.

#### POSTOPERATIVE MANAGEMENT

With proper preoperative care and attention to replacement of blood lost during the operative procedure, shock is seldom encountered. It

TABLE 2.—Percentage of Five-Year Survivals Conforming to Grade "A."

No. of Cases	Died from Operation	Died Within 5 Years			Untraced	Alive at 5 Years	Percentage of 5 Year Cures
		From Other Causes	of Cancer				
20.....	1	2	1		2	14	93.3%

has been our experience that whole blood is much more efficient in the prophylaxis and treatment of shock than plasma. In recent years, nutrition of the surgical patient from a postoperative standpoint has assumed a position of paramount importance. Intensive research has resulted in the discovery of protein hydrolysates which can be administered parenterally.<sup>11</sup> Similar advances have been attained in the field of parenteral administration of vitamins, and our knowledge of water and electrolyte balance has been materially extended.<sup>12</sup> Attention

11. Elman, R.: Amino Acid Content of the Blood Following Intravenous Injection of Hydrolyzed Casein, *Proc. Soc. Exper. Biol. & Med.* **37**:437 (Dec.) 1947.

12. Limbert, E. M.; Power, M. H.; Pemberton, J. D., and Wakefield, E. G.: Effects of the Parenteral Administration of Fluids on the Metabolism of Electrolytes During Postoperative Convalescence, *Surg., Gynec. & Obst.* **80**:609, 1945. Moyer, C. A.: Fluids and Electrolyte Balance, *Surg., Gynec. & Obst.* **84**:586, 1947. Yeomans, J. B.: Nutritional Deficiencies, Philadelphia, J. B. Lippincott Company, 1941, p. 233. Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema, *Arch. Surg.* **27**:159 (April) 1933. Hartzell, J.; Winfield, J. S., and Irvin, J. L.: Plasma, Vitamin C, and Serum Proteins in Wound Disruption, *J. A. M. A.* **116**:669 (Feb. 22) 1941.



enumeration of the indications for proctosigmoidectomy or the delineation of the areas to which it must be restricted, it might be in order to discuss the incidence of cancer in the lower part of the bowel, lymphatic spread and the blood supply to that area. In an effort to determine the precise location of the lesion in the bowel, records of 180 consecutive patients were studied, and the following data were obtained:

Location of Lesion	Patients
Sigmoid .....	23
Rectosigmoid .....	53—33.8%
	80.3%
Rectum (excluding lower 3 cm.).....	73—46.5%
Anal canal (including lower 3 cm. of rectum).. Total .....	31—19.7% 180

On the assumption that lesions in the sigmoid are resected solely by an abdominal approach and those located in the lowest 3 cm. of the rectum and anal canal by a method necessitating removal of the sphincters, there remain 80.3 per cent in which the sphincters may be preserved, if the findings in recent histopathologic investigations merit acceptance.

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has been called to the important part that protein metabolism, particularly in regard to hypoproteinemia, plays in the preparation and after-care of patients undergoing operation for a malignant tumor of the lower part of the bowel.<sup>13</sup> It is essential that an attempt be made post-operatively to maintain a positive nitrogen balance. In our patients, this is accomplished by the use of plasma, whole blood and from 60 to 120 Gm. of protein hydrolysate daily. In the estimation of fluid requirements, it is necessary to consider the average daily intake (2,500 to 3,500 cc.) and the loss of fluids from the body, i. e., the estimated loss from both the kidneys and the gastrointestinal tract and in addition that from Wangensteen suction, as well as the insensible loss from the skin and the lungs. In our experience, the urinary output has proved to be the most valuable index of the status of body water balance. In conjunction with this, the erythrocyte count, hemoglobin content, hematocrit value, serum protein, carbon dioxide content, serum chloride and urinary chloride and the specific gravity, together with the urinary  $p_H$ , are necessary determinants of rational fluid replacement. All fluid losses from suction, ileostomy or the presence of a fistula must be computed and replacement of similar electrolytic substances instituted. Attention should be invited to the danger of intoxication with salt, since it has been demonstrated that patients tolerate poorly any large amount of salt during the early postoperative periods.<sup>14</sup>

*Postoperative Ileus.*—After abdominal operations, a varying degree of temporary paralysis of the bowel is present. The condition is usually referred to as “physiologic ileus,” and its severity is in direct proportion to the degree of injury sustained by the viscera and peritoneum. When infection or further peritoneal irritation, such as leakage from the bowel anastomosis, is superimposed on this condition, the result is adynamic ileus. In either condition, intestinal stasis occurs, with the resultant accumulation of gas and fluid in the intestinal tract. Fully 60 per cent of intestinal gas is swallowed, and large amounts of fluid are secreted into the stomach and the small intestine. It is obvious, then, that gastroduodenal suction should be instituted immediately after abdominal operations to prevent intestinal distention until motility of the bowel returns. Its advantage in instances of postoperative adynamic or dynamic ileus is also well recognized. In cases of the adynamic type as well as the dynamic type occurring postoperatively with no evidence of circulatory disturbance, the Miller-Abbott tube or one of its variations has proved beneficial. Experience in the use of the tube is necessary to achieve

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13. Lund, C. C., and Levenson, S. M.: Protein in Surgery, J. A. M. A. **128**:95 (May 12) 1945.

14. Maddock, W. G., and Collier, F. A.: Water Balance in Surgery, J. A. M. A. **108**:1 (Jan. 2) 1937. Collier, F. A.; Campbell, K. M.; Vaughan, H. H.; Job, V., and Moyer, C. A.: Postoperative Salt Intolerance, Ann. Surg. **119**:533, 1944.

the best results, and there should be constant observation to see that it is functioning properly. Prophylaxis is the best treatment for ileus, including routine postoperative gastric or intestinal suction and the use of high concentrations of oxygen.

*Thromboembolism.*—Since the introduction of the newer antibiotics and sulfonamide compounds, death from infection is the exception rather than the rule. Because of this fact, the attention of surgeons has been drawn to other less frequent causes of death. Thus, an unprecedented interest has arisen in the thromboembolic diseases.<sup>15</sup> Although not at first apparent, justification for this is demonstrated in our series of 439 operative procedures on the bowel, in which 5 deaths occurred from pulmonary embolism. For a period of over two years a rigid prophy-

TABLE 3.—Data on Thromboembolism

Operations on the Bowel (Largely Abdominoperineal Proctosigmoidectomies)		Fatal Pulmonary Emboli	Mortality, Percentage
Prior to August 1945—439.....		5	1.1
Subsequent to August 1945—390.....		1	0.2
Prophylactic Measures		Indications for Anticoagulant Therapy	
1. Early exercises of legs hourly when awake		1. Tenderness over deep calf veins:	
2. Early unassisted movement in bed		(a) Homan's sign. (b) Moses' sign (New	
3. No pillows under knees		England J. Med. <b>234</b> : 288, 1946)	
4. Vigilant daily examinations for early signs		2. Unexplained concomitant rise in tempera-	
of deep venous thrombi of lower extremi-		ture and pulse	
ties		(a) Allen's sign	
5. Early ambulation, 2 to 5 days, depending		3. Previous embolic phenomena	
on operation		4. Evidence of superficial or deep thrombo-	
6. Elastic bandages for selected patients		phlebitis	
		5. Circulatory disturbance of lower extremi-	
		ties	
		6. Cardiac disease	
Therapy: Combination of heparin and "dicumarol."			

lactic regimen has been instituted, the results from which are given in table 3.

*Atelectasis.*—This condition is one of the most common of post-operative complications in our experience and becomes manifest early by a sharp rise in temperature. The diagnosis is usually not too difficult clinically if attention is paid to the increased respirations, chest lag on the affected side, decreased breath sounds and shifts of the heart and trachea. Adequate roentgenograms, and not bedside films, are diagnostic. Treatment should be immediate removal of the bronchial

15. Homans, J.: Venous Thrombosis in the Lower Limbs; Its Relation to Pulmonary Embolism, *Am. J. Surg.* **38**:313, 1937. Allen, A. W.; Linton, R. R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism: Further Experience with Thrombectomy and Femoral Vein Interruption, *J. A. M. A.*, **128**:397 (June 9) 1945. Detakats, G., and Fowler, F. F.: The Problem of Thrombo-Embolism, *Surgery* **17**:156, 1945.

obstruction by either suction with an intratracheal catheter or bronchoscopy.

*Genitourinary Complications.*—Postoperatively, continuous drainage of the bladder and frequent irrigations are used until vesical function has returned to normal as evidenced by cystometric studies and the amount of residual urine present. Transurethral resection has been unnecessary.<sup>16</sup>

*Wound Complications.*—Concerning the care of wounds and wound complications, it may be stated that with the use of stainless alloy steel wire for closure and the concomitant use of sulfonamide drugs and antibiotics the incidence of complications has been reduced to a minimum.

In general, the morbidity compares favorably with that for one or the other type of resection. Customarily the patient is permitted out of bed on the fifth postoperative day and discharged on the eleventh day. Ordinarily, he returns to his active pursuits between six and ten weeks after operation.

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16. Bacon, H. E., and McCrae, L. E.: Abdominoperineal Proctosigmoidectomy for Rectal Cancer: Management of Associated Vesical Dysfunction, J. A. M. A. **134**:523 (June 7) 1947.

# CARCINOMA OF THE COLON AND RECTUM

## A Ten Year Study

JOHN H. GARLOCK, M.D.

AND

SAMUEL H. KLEIN, M.D.

NEW YORK

IN JANUARY 1943<sup>1</sup> there was published from this service a paper discussing the complications and mortality following radical operations for cancer of the colon and rectum. The present communication represents in part a continuation of that study and includes an appraisal of the surgical therapy of this disease in a modern urban medical center, with the greater importance being paid to the operative mortality and to long term follow-up studies.

It was originally intended to report on the patients treated on the ward service only. However, as time went on during this study, it became clear that it would be of considerable interest if we included a comparable series of cases from the private practice of one of us (J. H. G.), in order to emphasize certain features which became evident as the analysis of the two series progressed. The combined series comprises a total of 910 cases, 549 from the ward service and 361 among the private group.

In the paper alluded to a statement was made, which, in the light of added experience, seems important enough to repeat at this time.

It is important to stress that many of the patients admitted to the wards of the Mt. Sinai Hospital do not represent the best physical material for major surgical procedures. Serious cardiovascular disease is common, as are diabetes and kidney disease. Many of the patients have led sedentary lives with little physical exercise, with the result that muscle tone is poor and the speed of recuperation is greatly reduced. Nutritional disturbances are common and there is great susceptibility to pulmonary infections. We are convinced that these factors are of considerable importance in influencing the mortality of major abdominal surgery in a large group of cases. There is a great difference in the physical status of ward patients living in large urban centers and those coming from rural communities. We do not believe that this has been stressed sufficiently in the past and that it may be an important reason for the disparity in the operative mortality statistics reported from various sections of the country.

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From the Surgical Service of the Mount Sinai Hospital.

Presented at the New York Surgical Society, Jan. 14, 1948.

1. Garlock, J. H.; Ginzburg, L., and Glass, A.: Complications and Causes of Mortality of the Surgical Treatment of Carcinoma of the Colon and Rectum, Surg., Gynec. & Obst. **76**:51-59 (Jan.) 1943.

In spite of the most modern methods of preoperative preparation, with great care paid to the patient's protein, electrolyte, mineral and vitamin needs, and in spite of the great advance in recent years along the lines of antibiotic therapy, we believe that this statement still holds true. There is no doubt that there has been an appreciable reduction of operative mortality all over the country since the need for careful preoperative preparation was generally appreciated. The advent of the antibiotics has played a great part in the progress of gastrointestinal surgery in the past decade, but in spite of this, there are many intangible factors which influence to a great extent the morbidity and mortality in the group of patients under consideration in this article. A careful study of the two comparative series emphasizes this fact most clearly.

In order to minimize and in part overcome the complicating medical disabilities enumerated, we formulated ten years ago a plan of preoperative rehabilitation, surgical procedure and postoperative care which we have continued during the years with certain modifications as experience increased. The preoperative period of preparation was frequently prolonged for two to three weeks to overcome anemia and nutritional disturbances and to treat cardiovascular disabilities and renal complications. In the majority of instances it was necessary to employ staged operative procedures. Finally, great attention was paid to the details of the postoperative care, which was found to equal in importance the preoperative period of rehabilitation.

With this plan it soon became evident that our incidence of operability increased. Operability and mortality are closely related. Factors which influence operability have a direct bearing on mortality. It has been amply demonstrated in many clinics that by extending the scope of operability the mortality rate increased, but with a proportionate increase in the number of patients surviving the five and ten year periods. These facts have influenced us in accepting for radical procedures patients who might otherwise have been rejected for fear of an increase in the operative mortality. Except in rare instances and in unusual circumstances, our index of operability has not been influenced by such considerations as age of the patient, obesity, loss of weight, anemia or associated chronic diseases. However, we are particularly wary of the patient who has had recent coronary thrombosis. It has been our experience that such patients withstand radical operations poorly. In general, it may be said that our index of operability has been influenced much more by conditions associated with the growth per se, such as fixation to neighboring vital structures and extensive hepatic metastasis. In many instances, operability was extended by the radical removal of involved contiguous organs such as a loop of small bowel, posterior wall of the bladder, uterus, vagina or adnexae or a portion of the abdominal wall.

The extent of lymph node involvement influences operability to a great degree, and the decision to perform a radical operation will rest, first, on the resectability of the involved nodes, second, on the accuracy with which the cause of the enlargement of nodes (neoplastic or inflammatory) is interpreted and, third, on the experience and boldness of the surgeon. The finding of metastasis to the liver at the time of exploration renders the situation hopeless, of course, from the standpoint of cure. However, with the knowledge that the patients with hepatic involvement not infrequently survive for as long as three years, it is justifiable to perform a resection of the colon for an operable local tumor, especially if it is producing obstructive symptoms or if the tumor is a large infected one, as is frequently found in the right colon.

It is not our purpose in this communication to describe in detail the methods utilized to rehabilitate many of the patients before operation. The majority of the patients in this series have been prepared for a period of five to seven days. The routine preparation consists of the use of a low residue intake, initial cleansing of the bowel with mild purgation, colonic irrigations, the administration of succinylsulfathiazole or phthalylsulfathiazole and the liberal use of blood transfusions preoperatively when indicated. Complicating medical disabilities are treated accordingly. Frequent use has been made of the Miller-Abbott tube when contemplating intestinal anastomosis.

In cases of acute intestinal obstruction due to carcinomas of the colon, recourse has been made to the operation of an exteriorized cecostomy. It is well known that colonic distention cannot be adequately relieved by the use of the Miller-Abbott tube alone. The Miller-Abbott tube will decompress the small bowel only, and there will remain a distention of the colon between the ileocecal valve and the obstructing tumor. Ill advised prolonged use of the Miller-Abbott tube in the hope that decompression of the large bowel will take place may lead to perforation of a markedly distended cecum. We should also like to stress the fact that no operative maneuvers should be carried out on the tumor-bearing portion of the bowel in the presence of an acute or subacute intestinal obstruction. If the surgeon at the time of exploration is confronted by a markedly distended large bowel proximal to the tumor, he should be content to limit the operative maneuver at this stage to a decompressing procedure and to defer his resection for a later date.

There has been no routine anesthesia in this group of patients. In the majority of instances, general anesthesia has been administered in the form of carbon dioxide, oxygen and ether or cyclopropane or ethylene and ether. Some of the members of the service have used spinal anesthesia, frequently of the continuous type. The choice of the anes-



thetic agent has, in the majority of cases, been delegated to the anesthetist. An effort has been made to individualize the patients and to pick the anesthetic agent for the particular problem at hand. In the same way, we have chosen a particular operative procedure to take care of the individual problem presented by each patient. Individualization of the patient has been the prime consideration at all times.

#### ANALYSIS OF CASES

We have arbitrarily divided the patients in this series according to anatomic sections of the colon and rectum. In each group we present comparative figures from the ward service and from the private group (table 1).

*Carcinoma of the Right Side of the Colon.*—Among the ward group there were 93 patients in this category, as opposed to 54 patients in

TABLE 1.—*Carcinoma of the Colon and Rectum*

<b>Ward Series</b>	
Right side of colon (cecum, ascending colon and hepatic flexure)....	93 (16.9%)
Transverse colon .....	27 (4.9%)
Splenic flexure .....	19 (3.5%)
Descending colon and sigmoid colon.....	145 (26.4%)
Rectosigmoid colon and rectum.....	265 (48.3%)
<b>Total .....</b>	<b>549*</b>
<b>Private Series</b>	
Right side of the colon.....	54 (14.9%)
Transverse colon .....	27 (7.5%)
Splenic flexure .....	9 (2.5%)
Descending colon and sigmoid colon.....	109 (30.2%)
Rectosigmoid and rectum.....	162 (44.9%)
<b>Total .....</b>	<b>361†</b>

\* The number of patients was 544. The lesions include six "double" lesions, necessitating multiple resection operations (table 2).

† The number of patients was 361. There was 1 "double" carcinoma, requiring multiple resection operations—one stage ileocolic resection for carcinoma of the right colon and obstructive resection for carcinoma of the transverse colon.

the private series (tables 2 and 3). In the ward group there were 62 operable cases, an operability rate of 66.7 per cent. This is to be compared with a rate of 81.5 per cent in the private series (table 2). In the first group the operative mortality in the cases of resectable tumors was 8.1 per cent, and in the second group it was 6.8 per cent. The accompanying tables indicate the subdivision for the one and two stage operations. It has been our experience that many patients with tumors on the right side are in a markedly depleted condition when admitted to the hospital, usually with a severe secondary anemia simulating, sometimes, pernicious anemia and associated with considerable disturbances in the protein metabolism. In spite of adequate and thorough preoperative rehabilitation, our experience has indicated that it is wiser in the majority of instances to stage the resection, the first operation consisting of an ileotransverse colostomy with exclusion of the ileum, and the second stage, performed approximately three weeks

TABLE 2.—*Carcinoma of the Right Side of the Colon*

Ward Series	
Total number of cases—93	
A. Operable.....	62 (66.7%); (5 deaths—8.1% mortality)
Procedures performed:	
(a) One stage ileocelectomy.....	12 (2 deaths—16.7%)
(b) Staged procedures	
1. Ileocolostomy with exclusion; ileocolic resection.....	47 (1 death—2.1%)
2. Ileocolostomy with exclusion (first stage of proposed two stage resection).....	1 (1 death)
3. Ileocolic obstructive resection.....	2 (1 death)
Total.....	50 staged procedures (3 deaths—6.0% mortality)
Causes of Death	
1. Multiple abscesses of the liver (autopsy)	
2. Intestinal obstruction (autopsy)	
3. Pneumonia (no autopsy)	
4. Sulfanilamide hepatitis (no autopsy)	
5. Cause not clear (no autopsy)	
B. Inoperable .....	31 (33.3%)
Procedures performed	
(a) Exploratory laparotomy .....	3
(b) Palliative operations.....	28 (7 deaths—25.0% mortality)
Private Series	
Total number of cases—54	
A. Inoperable group.....	10 (18.5%)—palliative ileocolostomy with exclusion performed. No postoperative deaths
B. Operable group.....	44 (81.5%)
(a) One stage ileocolic resection.....	22; postoperative deaths, 2 (9.1%)
(b) Two stage ileocolic resection.....	22; postoperative deaths, 1 (4.5%)
Combined mortality of groups a and b.....	6.8%
Causes of Death	
1. Coronary artery occlusion	
2. Local peritonitis due to slough of inverted end of colon	
3. Cause undetermined	

TABLE 3.—*Carcinoma of the Transverse Colon*

Ward Series	
Total number of cases—27	
Operable group.....	16 cases (59.3%); 2 deaths (12.5% mortality)
Procedures performed	
Resection and primary anastomosis; complementary cecostomy.....	1
Primary ileosigmoidostomy with exclusion; secondary right hemicolectomy...	2
Primary obstructive resection; secondary spur crushing and colostomy closure...	11
Obstructive resection .....	1
(died; clinical picture of cerebrovascular accident and terminal pneumonia; no autopsy)	
Ileotransverse colostomy with exclusion.....	1
(died; clinical picture of uncontrollable gastric hemorrhage; autopsy: peptic ulcer and pulmonary embolism)	
Inoperable group.....	11 cases (40.7%)
Exploratory laparotomy .....	3
Palliative procedures .....	8
Cecostomy .....	2
Ileosigmoidostomy.....	4 (1 death; autopsy: bronchopneumonia)
Primary cecostomy, for obstruction; secondary ileosigmoidostomy.....	1
Primary cecostomy, for obstruction; secondary exploratory laparotomy (inoperable) .....	1
Private Series	
Total number of cases—27	
Inoperable group .....	5 (18.5%)
Procedures performed	
(a) Exploratory laparotomy .....	2
(b) Palliative procedures .....	3
(obstructive resection, 1; ileosigmoidostomy with exclusion, 2)	
(no postoperative deaths)	
Operable group .....	22 (81.5%)
Procedures performed	
(a) Obstructive resection .....	21
(b) Resection with end to end anastomosis.....	1
(no postoperative deaths)	

later, consisting of an ileocolic resection. Study of the accompanying charts will indicate the marked difference in operative mortality, with the single and two stage operations, in the ward group 16.7 per cent for the one stage ileocelectomy and 6 per cent for the staged operation. In the private series, the comparative figures are 9.1 and 4.5 per cent. The argument has been frequently advanced that the two stage operation offers the patient two chances to die and therefore the one stage operation should be done in the majority of instances. Our experience has been in direct contradistinction to this thought. In the combined group of 72 patients subjected to the two stage operation only 1 patient died after the first procedure. A study of table 2 will indicate the causes of death in the operable group of the two series and the findings when permission for postmortem examination was obtained.

*Carcinoma of the Transverse Colon.*—In this group there were 27 patients in the ward group and 27 in the private group. The operability in the first was 59.3 per cent and in the second 81.5 per cent. Table 3 will indicate the procedures carried out in both the operable and the inoperable groups of both series. It will be noted that the vast majority of radical procedures consisted of obstructive resections, with the formation of a double-barreled colostomy opening which was closed at a later date. This brings up the general problem of obstructive resection as opposed to resection with primary anastomosis, which is now being carried out with increasing frequency throughout the country. To go into this problem extensively would carry us far afield and beyond the original intent of this paper. Suffice it to say that when the study of the problem of carcinoma of the colon was begun on this service, the necessity for staged procedures soon became evident. After the general adoption of the staged operation program, there was noted a pronounced reduction in the operative mortality. Since the advent of the sulfonamide compounds for intestinal antisepsis and the more general appreciation of the great need for careful pre-operative rehabilitation, there has been an increased tendency throughout the country to return to the operation of resection and anastomosis which was practiced by many of the surgeons more than a quarter of a century ago. We all find that we are increasing our number of cases of primary anastomosis as time goes on, but we should like to emphasize that the operation of obstructive resection is still an excellent one, is a good operation for cancer and carries with it a commendably low mortality rate. In addition, our experience indicates that there is a vast difference in the smoothness of the postoperative course of the two types of operation. Our morbidity following obstructive resection has been much less than with the operation of primary anastomosis. We have set down definite criteria for the use of this operation. We

believe that it should not be carried out in the following circumstances: (1) when there is any evidence of obstruction proximal to the tumor; (2) when there is marked obesity of the patient, with infiltration of fat in the mesentery of the bowel; (3) when patients in the older age groups are being dealt with, on whom it is important to carry out a rapidly executed procedure so that they can be taken off the operating table as soon as possible, and (4) in the presence of pericolic infection.

If none of these complicating factors is present, we believe that it is safe to carry out the operation of resection and primary anastomosis supplemented by a proximal decompressing tube cecostomy. The purpose of the cecostomy is to prevent gaseous distention of the colon in

TABLE 4.—*Carcinoma of the Splenic Flexure*

		Ward Series
Total number of cases—19		
Inoperable group		5 (26.3%)
Procedures performed		
(a) Exploratory laparotomy		1
(b) Palliative operations		3 (2 deaths)
(Cecostomy for obstruction; patient died; autopsy showed peritonitis secondary to perforation of the obstructed colon.		
Ileosigmoidostomy with exclusion; patient died; autopsy showed peritonitis secondary to perforation of the tumor		
Obstructive resection)		
Operable group		14 (73.7%); 2 deaths (14.3%)
Procedures performed		
(a) Obstructive resection		10
(2 deaths. One patient died suddenly on the 11th postoperative day with pulmonary embolism (?), pulmonary thrombosis (?); no autopsy. The other had profuse bleeding from the proximal colostomy limb; no autopsy)		
(b) Primary cecostomy for obstruction, secondary to obstructive resection		4
		Private Series
Total number of cases—9		
Inoperable group		2 (22.2%)
Procedures performed: obstructive resection		
(no deaths)		
Operable group		7 (77.8%)
Procedures performed: obstructive resection		
(no deaths)		

the region of the anastomosis. It can be done quickly at the same sitting or, if necessary, as a preliminary procedure. The mortality for the operable cases was 12.5 per cent in the ward series; there were no deaths in the private group (table 3).

*Carcinoma of the Splenic Flexure.*—We believe that cases of carcinoma of the splenic flexure should be specially considered because of the inherent technical difficulties associated with operative resections in this region. The old writers emphasized the high mortality associated with resection for this condition. There were 19 cases in the ward group and 9 in the private group. The operability rate was 73.7 per cent in the first as opposed to 77.8 per cent in the second. In the operable group the mortality figures were 14.3 per cent and zero respectively. Table 4 indicates the essential features of the two groups.

*Carcinoma of the Descending Colon and the Sigmoid Colon.*—In the ward series there were 145 patients as compared with 109 in the private series. There were 4 patients in the ward group who under-

TABLE 5.—*Carcinoma of the Descending and Sigmoid Portions of the Colon: Postoperative Mortality in the Ward Series*

(Total number of cases: 145)	Number of Cases	Deaths	Mortality, %
A. Inoperable group .....	49 (33.8%)	10	20.4
B. Questionably operable group.....	4 (2.8%)	4	100.0
C. Operable group .....	92 (63.4%)	6	6.5
Group B plus group C.....	96 (66.2%)	10	10.4

TABLE 6.—*Carcinoma of the Descending and Sigmoid Portions of the Colon: Operable Group in the Ward Series.*

A. Obstructive resection.....	88 cases (7 deaths—7.95% mortality)
B. Resection and end to end anastomosis.....	3 cases
1 case {	(a) Preliminary decompressive colostomy
	(b) Resection of neoplasm and involved adherent small bowel and anastomosis
	(c) Closure of primary colostomy
2 cases {	(a) Preliminary decompressive colostomy
	(b) Resection of neoplasm and anastomosis
	(c) Closure of primary colostomy
C. Sigmoidotomy and excision of adenomatous polyp showing carcinomatous degeneration .....	1 case

TABLE 7.—*Carcinoma of the Descending and Sigmoid Portions of the Colon: Mortality in Obstructive Resection Group*

{(a) Decompressive cecostomy	Died 4th postoperative day;	High intestinal obstruction
{(b) Obstructive resection	no autopsy	developed after last operation;
{(c) Closure of colostomy		jejunostomy performed
{(d) Closure of cecostomy		
Obstructive resection	Died suddenly 5th postoperative day; no autopsy	Clinical picture of acute coronary occlusion; patient known preoperatively to have severe myocardial damage
Obstructive resection and drainage of pelvic abscess	Died on 43rd postoperative day; autopsy: pituitary tumor, bronchiectasis and bronchopneumonia, emphysema, atelectasis and purulent bronchitis; cardiac hypertrophy	First week pneumonia and cardiac failure; fifth week convulsions and coma
Obstructive resection	Died on 12th postoperative day; autopsy: pulmonary embolism	
Obstructive resection	Died on 29th postoperative day; autopsy: acute right pyelonephritis, acute suppurative bronchopneumonia of lower lobe of left lung	Auricular fibrillation, pneumonia, bacteremia and ascending urinary infection clinically
{(a) Decompressive cecostomy	Died on 3rd postoperative day	Autopsy: pulmonary embolism, peritonitis localized around colostomy; hypernephroma on left side
{(b) Obstructive resection		
Obstructive resection and resection of loop of involved ileum	Died on 8th postoperative day	Autopsy: intestinal occlusion; bronchopneumonia

went primary decompressing cecostomy for acute intestinal obstruction but who died before coming to the second procedure. We are therefore unable to determine whether theirs were operable tumors. If these

are excluded then the operability rate in this group was 63.7 per cent. If they are to be included, the rate becomes 66.2 per cent. In the group of 109 private patients the operability rate was 77.1 per cent. Tables 5 to 8 bring out clearly the details of the operations performed in both series. The operative mortality in the ward series for the operable group was 6.5 per cent. If the 4 patients described previously are included in the calculation, then the gross mortality for this group

TABLE 8.—*Carcinoma of the Descending and Sigmoid Portions of the Colon in the Private Series*

Total number of cases—109	
A. Inoperable group .....	25 (22.9%)
Procedures performed	
(a) Exploratory laparotomy .....	3
(b) Palliative operations	
1. Colostomy .....	3
2. Obstructive resection .....	18
(1 postoperative death due to peritonitis)	
B. Operable group.....	84 (77.1%; postoperative mortality, 1.2%)
Procedures performed	
(a) Obstructive resections .....	80
(including 1 case with partial resection of bladder; no deaths)	
(b) Resection with end to end anastomosis.....	3 (no deaths)
(c) Cecostomy for acute descending colon obstruction.....	1
(this patient died postoperatively; autopsy: chronic ulcerative colitis, perforation of the carcinoma with abscess formation and peritonitis)	

TABLE 9.—*Ward Series: Carcinoma of the Rectosigmoid Colon and the Rectum (265 Cases)*

Inoperable group .....	76 (28.7%)
Postoperative deaths .....	19 (25%)
Procedures performed	
A. Exploratory laparotomy..9 (1 death [11.1%]; autopsy: pulmonary embolism)	
B. Palliative procedures.....	67 (18 deaths, 28.9%—table 16)
Colostomy .....	58
Resection of gangrenous sigmoid volvulus about rectosigmoid carcinoma..	1
Obstructive resection .....	2
Anterior resection .....	2
Primary colostomy; secondary enterostomy for peritonitic ileus.....	1
Two stage abdominoperineal resection.....	1
Colostomy and resection (and anastomosis) of small bowel loop.....	1
Drainage of pelvic abscess and peritonitis.....	1

becomes 10.4 per cent. In the private series the postoperative mortality was 1.2 per cent.

*Carcinoma of the Rectosigmoid and the Rectum.*—Cases of this constitute the largest group in the entire series. Among the ward cases there were 265, and the private cases totaled 162. The operability rate in the ward group was 71.3 per cent as compared with 91.3 per cent in the private series. Tables 9 to 13 indicate the various procedures that were utilized in the operative therapy of this disease. The comparable general operative mortality was 21.2 and 8.8 per cent. The accompanying tables also indicate the comparable mortality in the two

groups following each type of operation. It is interesting to note that the mortality following abdominoperineal resections is noticeably higher than that following the operation of anterior resection with anastomosis.

TABLE 10.—*Surgical Procedures Performed for Carcinoma of the Rectosigmoid Colon and the Rectum in the Ward Series (189 Cases [71.3 %])*

Abdominoperineal resection

A. One stage "combined" operation.....	118
(including 1 case in which disconnection of the mechanism of a previous ileosigmoidostomy which had been done elsewhere and ileocolostomy were performed)	
B. Staged procedures	
1. First stage: decompressive colostomy for obstruction } .....	4
Second stage: abdominoperineal resection.....	
2. First stage: obstructive resection of carcinoma of rectosigmoid (colostomy not closed } .....	1
Second stage: abdominoperineal resection of carcinoma of rectum.....	
3. Lahey type two stage abdominoperineal resection (including 3 cases in which total hysterectomy was performed because of neoplastic invasion).....	17
4. Miscellaneous	
(a) Diffuse polyposis of the colon and carcinoma of the rectum.....	1
First stage: ileostomy	
Second stage: abdominoperineal resection	
Third stage: total colectomy	
(b) Polyposis of left half of colon and carcinoma of the rectum.....	2
First stage: ileostomy	
Second stage: hemicolectomy to rectosigmoid	
Third stage: hemicolectomy to rectosigmoid	
Fourth stage: abdominoperineal resection	
First stage: abdominoperineal resection	
Second stage: left hemicolectomy	
C. Hartmann procedure .....	4
(in 1 case included partial cystectomy, suprapubic cystostomy and total resection of uterus and adnexa)	
D. Obstructive resection (carcinoma of rectosigmoid colon).....	3
(in 1 case included partial cystectomy)	
E. Colotomy and local excision of villous adenoma of rectosigmoid colon, showing carcinomatous transformation .....	1
F. Local excision of villous adenoma of rectum showing foci of carcinomatous transformation .....	1
G. Colostomy .....	4
3 cases, first stage of proposed Lahey operation	
1 case, first stage of proposed Lockhart-Mummery operation	
H. Anterior resection, with end to end anastomosis.....	19
First stage: decompressive colostomy for obstruction.....	4 cases
Second stage: anterior resection with end to end anastomosis.....	
Third stage: closure of colostomy.....	
First stage: elective preliminary diverting colostomy.....	1 case
Second stage: anterior resection with end to end anastomosis.....	
Third stage: closure of colostomy.....	
First stage: anterior resection with end to end anastomosis and complementary transverse colostomy .....	11 cases
Second stage: closure of colostomy.....	
(a) 1 case in which obstructive resection of a splenic flexure carcinoma had been done five weeks previously	
(b) 1 case in which two stage ileocolostomy for carcinoma of ascending colon had been done five weeks previously	
(c) 1 case in which two stage ileocolostomy had been done for carcinoma of ascending colon four years previously	
First stage: anterior resection with end to end anastomosis and complementary sigmoid colostomy .....	3 cases
Second operation: Perineal presacral incision and drainage for infection	
Second stage: closure of colostomy.....	
I. Lockhart-Mummery resection .....	14
(a) Preliminary colostomy	
(b) Secondary perineal resection	

It will be noted by a careful perusal of table 11 that we have been fortunate in obtaining permission for autopsy in a high percentage of cases in the ward series. In the total group of 40 deaths, there were

TABLE 11.—*Causes of Death in the Operable Group with Carcinoma of the Rectosigmoid Colon and the Rectum in the Ward Series*

Cause of Death	No		Total
	Autopsy	Autopsy	
Shock .....	..	1	1
Coronary artery occlusion.....	1	..	1
Pneumonia .....	7	..	7
Pneumonia and peritonitis.....	1	..	1
Peritonitis .....	7	1	8
Myocardial failure .....	4	..	4
Cerebrovascular accident .....	2	1	3
Acute intestinal obstruction.....	1	2	3
Pulmonary embolism .....	3	1	4
Massive hemorrhage from duodenal ulcer.....	1	..	1
Pulmonary atelectasis .....	1	..	1
Hemoglobinuric renal degeneration (transfusion reaction)	1	..	1
Jaundice and paralytic ileus.....	1	..	1
Hepatic damage and coronary insufficiency.....	1	..	1
Peritonitis and pulmonary embolism.....	1	..	1
Miliary tuberculosis .....	1	..	1
Sepsis ( <i>Staphylococcus aureus</i> ).....	1	..	1
Total .....	34	6	40

TABLE 12.—*Postoperative Mortality in the Operable Group with Carcinoma of the Rectosigmoid Colon and the Rectum in the Ward Series*

Procedures Performed	No. of Cases	Survived	Died	Mortality, %
Abdominoperineal resection .....	126	97	29	23.0
Lahey two stage abdominoperineal resection....	17	15	2	11.8
Lockhart-Mummery resection .....	14	12	2	14.3
Hartmann procedure .....	4	2	2	50.0
Colotomy and local excision.....	1	1	0	0
Local excision per rectum.....	1	1	0	0
Obstructive resection .....	3	3	0	0
Anterior resection .....	19	18	1	5.3
Colostomy .....	4	0	4	100.0
Total .....	189	149	40	21.2

TABLE 13.—*Carcinoma of the Rectosigmoid and Rectum in the Private Series*

Total number of cases—162

- A. Inoperable group .....14 (8.63%)  
 Procedures performed  
   (a) Exploratory laparotomy ..... 5  
     (1 postoperative death, due to intra-abdominal metastasis)  
   (b) Palliative operations.....9 (obstructive resection, 1; colostomy, 7; abdominoperineal resection, 1)
- B. Operable group .....148 (91.35%)  
 Procedures performed  
   (a) Abdominoperineal resection ..... 99  
     in one stage, 96 (10 deaths—10.4%) in two stages, 3 (no mortality)  
     combined mortality, 10.1%  
   (b) Anterior resection and anastomosis, with complementary temporary proximal colostomy.....37 (2 deaths) mortality, 5.4%  
   (c) Hartmann resection ..... 2  
   (d) Local excision per rectum of small adenomatous polyp showing early carcinomatous degeneration ..... 1  
   (e) Lockhart-Mummery resection ..... 2  
   (f) Obstructive resections .....7 (1 death—14.2%)
- Total.....148; deaths, 13 (8.8%)



8 instances of peritonitis, and of these, 7 were proved by postmortem examination. We might emphasize that this complication has been most unusual during the past four or five years. The majority of the deaths have been due mainly to complications caused by associated medical disabilities.

#### FOLLOW-UP STUDIES

In an urban center like New York city, with its constantly shifting population, it is difficult to follow patients for as long a period as is required for a study such as this. This was especially difficult during the war years. We were, naturally, able to obtain a higher percentage of late follow-up examinations in the group of private patients. This analysis has emphasized two important facts:

1. In the group of patients with lymph node involvement at the time of operation the curve of long term survivors falls rapidly as the years go by. The greatest number of survivors are in the group in which spread to lymph nodes does not occur.

TABLE 14.—*Carcinoma of the Colon and Rectum in Combined Total of Ward and Private Series (910 Cases)*

Mortality in the Operable Cases	Ward Series		Private Series	
	Operable Cases	Deaths	Operable Cases	Deaths
Right colon .....	62 (66.7%)	5 (8.1%)	44 (81.5%)	3 (6.8%)
Transverse colon .....	16 (69.3%)	2 (12.5%)	22 (81.5%)	0
Splenic flexure .....	14 (73.7%)	2 (14.3%)	7 (77.8%)	0
Descending colon and sigmoid colon....	96 (66.2%)	10 (10.4%)	84 (77.1%)	1 (1.2%)
Rectosigmoid colon and rectum.....	189	40 (21.2%)	148 (91.35%)	13 (8.8%)
	(Including 4 questionably operative cases—4 deaths)			
Total .....	377 (68.6%)	59 (15.6%)	305 (81.2%)	17 (5.6%)
	Combined group, 682 (74.9%); 76 deaths (11.1%)			

2. As the experience of the individual surgeon increases, he will undertake more radical resections, with a resultant increase in his rate of operability and a consequent increase in the number of long term survivors.

A study of tables 15 and 16 will indicate that the greatest number of survivors proportionately are in the groups with carcinoma of the right side of the colon and the rectum, in that order. It is possible that the prognosis for neoplasms of the right side is better because of the greater ease of more radical resections by virtue of the anatomy of the mesentery and its contained lymph nodes. However, there are certain pathologic features based on clinical operative experience which indicate fundamental differences between cancer on the right side and cancer on the left side. From the large experience indicated by the report in this paper, it is apparent that the neoplasms on the right side grow in a centrifugal or centripetal direction, with the formation, in the main, of large ulcerating tumors, and that cancerous lymph node spread is not nearly as frequent as with tumors on the left side.

TABLE 15.—Follow-Up of Operable Cases in Ward Series

	Lymph Node or Pericolic Involve- ment	Total	Known to Be Alive and Well (Years)											Died or Had Recur- rence
			0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	
Right side of colon														
1937-1942.....	—	15	1	..	..	..	1	3	2	..	2	1	..	2
	+	9	..	..	..	1	..	..	..	..	..	..	..	8**
1942-1947.....	—	24	2	6	1	2	1	..	..	..	..	..	..	10§§
	+	9	1	3	1	..	..	..	..	..	..	..	..	3
Transverse colon														
1937-1942.....	—	5	..	..	..	..	..	3	1	..	..	1	..	..
	+	3	..	..	..	..	..	..	..	..	..	..	..	3
1942-1947.....	—	6	1	2	..	..	1	..	..	..	..	..	..	1
	+	0	..	..	..	..	..	..	..	..	..	..	..	..
Splenic flexure														
1937-1942.....	—	5	..	..	..	..	..	..	..	..	2	..	..	3†
	+	1	..	..	..	..	..	..	..	..	..	..	..	1
1942-1947.....	—	4	1	3	..	..	..	..	..	..	..	..	..	..
	+	2	..	..	..	..	1	..	..	..	..	..	..	1
Descending and sigmoid portions of colon														
1937-1942.....	—	14	1	1	..	..	1	4	..	2	..	3	..	2§
	+	18	1	..	1	1	1	1	1	..	1	1	..	8
1942-1947.....	—	41	2	12	6	3	3	1	..	..	..	..	..	5
	+	13	2	1	2	..	..	..	..	..	..	..	..	7
Rectosigmoid colon and rectum														
1937-1942.....	—	36	..	..	3†	1	1	5	4	3	1	3	..	9
	+	30	2	..	1	1	..	1	2†	2	..	1	..	5
	Not known	3	..	..	..	..	..	..	..	..	..	..	..	2
1942-1947.....	—	57*	12*†	10	2	6	5	4	..	..	..	..	..	2
	+	22	4	4	4	3	..	..	..	..	..	..	..	4
	Not known	1	..	..	..	..	..	1	..	..	..	..	..	..

\* Includes leiomyosarcoma.

† Includes 1 melanocarcinoma.

\*\* One recurrence at six years and 1 at seven years.

§§ One died of pneumonia.

‡ There were two recurrences at five and one-half years, and 1 died at seven years eleven months.

§ One died at five years eight months, after gastrectomy for carcinoma of the esophagus, and 1 died at seven years, cause undetermined.

TABLE 16.—Follow-Up of Operable Cases in Private Series

	Lymph Node or Pericolic Involve- ment	Total	Known to Be Alive and Well (Years)											Died or Had Recur- rence
			0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	
Right side of colon														
1937-1942.....	—	4	..	..	..	..	1	1	..	..	..	1	..	..
	+	1	..	..	..	..	..	..	..	..	..	..	..	..
1942-1947.....	—	23	2	8	3	2	3	..	..	..	..	..	..	4
	+	13	5	1	1	1	1	..	..	..	..	..	..	4
Transverse colon														
1937-1942.....	—	0	..	..	..	..	..	..	..	..	..	..	..	..
	+	1	..	..	..	..	..	..	1	..	..	..	..	..
1942-1947.....	—	13	4	4	1	1	1	..	..	..	..	..	..	2
	+	8	2	2	..	..	..	..	..	..	..	..	..	4*
Splenic flexure														
1937-1942.....	—	2	..	..	1	1	..	..	..	..	..	..	..	..
	+	0	..	..	..	..	..	..	..	..	..	..	..	..
1942-1947.....	—	3	..	..	1	1	..	..	..	..	..	..	..	1
	+	2	..	..	..	..	..	..	..	..	..	..	..	2
Descending and sigmoid portions of colon														
1937-1942.....	—	11	..	..	..	1	1	1	3	..	1	..	1	2
	+	6	..	..	..	..	..	..	2	..	..	..	..	4
1942-1947.....	—	43	14	13	4	4	2	..	..	..	..	..	..	6†
	+	23	11	2	1	1	1	..	..	..	..	..	..	5
Rectosigmoid colon and rectum														
1937-1942.....	—	19	1	1	1	..	1	2	2	5	..	..	1	4
	+	8	..	..	..	..	..	1	..	1	..	..	..	6‡
1942-1947.....	—	69	28	12	8	3	2	1	..	..	..	..	..	14§
	+	39	7	2	5	3	..	1	..	..	..	..	..	21

\* One died of coronary thrombosis.

† One died suddenly, cause undetermined.

‡ One died (suicide).

§ Two died of coronary thrombosis, and 1 died of cerebral hemorrhage.

Enlargement of lymph nodes is frequently seen at the time of operation, but this is more likely to be found to be inflammatory. The converse is more often seen with tumors on the left side. It is interesting and heartening to note that of 36 patients in the ward group operated on for cancer of the rectum without involvement of the nodes in the 1937-1942 period 21 are alive and apparently free of disease, three to ten years later. In the same series, of 30 patients with metastasis to lymph nodes, 10 are alive for periods up to ten years. The follow-up studies for cancer in other parts of the colon yield figures which are slightly less promising.

The ward series of patients were operated on by a fairly large group of surgeons, including residents, young surgeons undergoing progressive training and the senior men on this service. During the war years, with a greatly curtailed and frequently inadequately trained staff, the situation was particularly difficult. Many of the deaths in the ward series occurred during this time. We believe that the figures presented constitute what one would find in any good general hospital in this country where operations are being carried out by average surgeons. During the years before the general employment of antibiotics, it was necessary to employ staged procedures and therefore the operation of obstructive resection for neoplasms of the left side was almost routine. We still believe that this is an excellent operation and that it should be taught to every resident surgeon. We are firmly convinced, from our rather extensive experience with this procedure, that as radical an operation can be effected as with the procedure of primary anastomosis.

If one mobilizes the splenic flexure and frees the descending colon from its lateral peritoneal attachments, it becomes an easy matter to remove large sections of the left colon and the accompanying mesentery. The same procedure is carried out when the operation of primary anastomosis is being performed. We are firm in our belief that for the average surgeon it is a much safer operation. If we can teach a large group of surgeons to do a good operation for cancer, with a lower mortality, we should not become exercised about the few extra days the patient must spend in the hospital. It seems to us that too much emphasis is being attached to this question of the time spent in the hospital. We believe that when the therapy of carcinoma is being dealt with the question of the days in the hospital needed to accomplish the surgeon's purpose is unimportant.

#### SUMMARY

There has been presented in this paper a series of 910 instances of cancer of the colon and rectum. The patients are divided into two comparable groups, one, 549 in number, treated on the ward service and the other, 361 in all, treated as private patients. The marked

difference in the operability rates and the operative mortality of the two groups emphasizes certain statements which were made in previous publications, namely, that there is a vast difference between the type of patient that one encounters in ward practice and the type encountered in private practice, that the private patient seeks aid at an earlier stage in his disease and that the results obtained by spreading out the ward material among a large group of surgeons in various stages of development more correctly approximate the general situation for this type of surgery throughout the country.

The data presented in this paper indicate that the operation of obstructive resection is still an excellent one and should not be discarded in the present wave of enthusiasm for the operation of resection and primary anastomosis. Criteria have been set down on the basis of which the latter procedure seems contraindicated.

Follow-up studies indicate that the greatest number of long term survivors are to be found in the group without lymph node involvement at the time of operation.

## PANCREATIC CYST

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IF PANCREATIC cyst were not an uncommon condition, it might be mistaken for carcinoma of the stomach more frequently. During the past twelve years there were 8 cases of pancreatic cyst and 596 cases of carcinoma of the stomach among a total of 160,011 patients admitted to Mercy Hospital, a ratio of 1:75:20,000.

Cysts may be classified into five major groups: (1) developmental—arising on the basis of congenital anomaly; (2) degenerative—the inflammatory-traumatic cyst or pseudocyst, comprising the majority of all pancreatic cysts; (3) obstructive—the small retention or mechanical cyst, the result of obstruction from stone, carcinoma or proliferation of the ductal epithelium; (4) proliferative—composed principally of cystadenoma and cystadenocarcinoma; (5) parasitic—caused by *Echinococcus* (hydatid).

### ANATOMY AND PRESENTATION OF CYSTS

The adult pancreas is an elongated, flattened, wedge-shaped structure lying in the transverse-oblique position in the posterior epigastric and hypochondriac regions. Because of the unyielding nature of the vertebral column and the posterior upper end of the abdominal cage, any cystic mass developing in the pancreas will tend to point anteriorly in the line of least resistance and the symptoms and signs will depend on the size of the mass and the pressure displacement of adjacent organs.

The pancreas is divided regionally into head, neck, body and tail. A cyst arising in the head encroaches primarily on the first and second portions of the duodenum, producing widening of the duodenal loop; with further enlargement it also presses on the pyloric and prepyloric areas of the stomach, the third part of the duodenum and the transverse colon (fig. 1*a*). If the cyst originates in the most lateral (right) portion of the head (fig. 1*e*), the first and second parts of the duodenum may be displaced medially and anteriorly, as occurred in the case reported in detail. A cyst arising in the short neck impinges directly on the posterior wall of the prepyloric region of the stomach

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(fig. 1*b*). If the point of origin is in the body of the pancreas, pressure is created anteriorly on the posterior wall of the middle portion of the stomach via the lesser peritoneal space and in a downward direction on the transverse mesocolon (fig. 1*c*). A cyst located in the tail of the gland displaces the greater curvature of the stomach, the duodenojejunal flexure and the first portion of the jejunum (fig. 1*d*). If large, the proximal loop of the splenic flexure of the colon also may be distorted.

In addition to the size and location of the cyst, much will depend on visceral conditions. Ptosis, obesity, adhesions, age, sex and concomitant or associated disease of other organs are modifying factors.

Cysts of the pancreas often attain considerable size before giving symptoms sufficiently annoying to cause the patient to seek medical

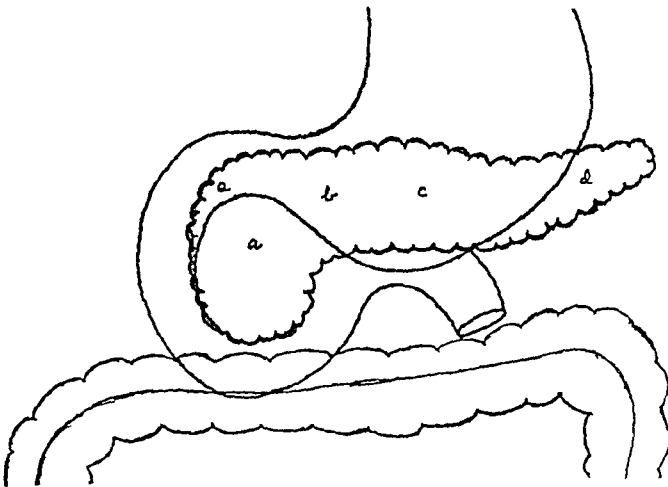


Fig. 1.—Schematic drawing showing relationship of pancreas to surrounding viscera; *a*, *b*, *c* and *d* represent head, neck, body and tail of gland. Solid organs have been omitted for simplicity.

attention, and discovery of cysts not sufficiently large to produce pressure symptoms is usually made incidentally at operation or autopsy.

#### ETIOLOGY

No single common factor serves to explain the etiology of all pancreatic cysts. Development of cysts has to do with the external secretory mechanism of the gland. Whereas other endocrine glands are small and compactly arranged, the pancreas assumes a much elongated shape, and its 12 to 20 cm. length (Borak; Gray) presents a longer duct system susceptible of involvement by disease or injury. In addition, it possesses no true capsule whose resistant quality might serve to confine the increasing pressure of accumulating cystic fluid.

Since degenerative cyst or pseudocyst is the most frequently encountered, as well as the most interesting from an etiologic point of view, three factors which may bear on its development will be considered. These factors are (1) anatomic, (2) inflammatory and (3) traumatic.

No conclusive evidence, clinical or experimental, has proved that obstruction of a main pancreatic duct results in cyst formation (Mahorner and Mattson; Pascucci). Experimental ligation of the main duct has resulted in fibrosis and some dilatation of distal small ducts, but no true cyst has formed (Opie). Likewise, the postulation that fibrosis of the gland results in constriction of main ducts, followed by dilatation of the distal ducts, degeneration of acinar cells and necrosis due to liberated ferments (Dieckhoff; Tilger) remains to be proved experimentally (Pinkham). However, there are considerable anatomic variations in the duct arrangements of the adult pancreatic gland, both within the gland itself and in the relationship of the main pancreatic duct to the common bile duct. Embryologically, the pancreas develops from two distinct portions, the dorsal and ventral, which fuse at about the seventh week of life. The dorsal portion becomes the entire adult gland, with the exception of a part of the head and the main duct (Wirsung's), which are ventral derivatives (Arey; Rienhoff and Pickrell). That such fusion often occurs in an incomplete manner has been emphasized by Rienhoff and Pickrell, who found no functioning connection between the main and accessory pancreatic ducts in 11 per cent and nonpatency of the duodenal opening of the accessory duct in 23 per cent of 100 autopsy specimens. Thus in 34 per cent of their cases secretion could not escape into the duodenum by way of the accessory duct in the event that the main duct was blocked. Such variations may not, in themselves, be responsible for alteration in function to a degree producing clinical symptoms, but when the factor of trauma or inflammation is superimposed, there is greater likelihood of a more severe pancreatitis and perhaps of subsequent development of a cyst.

The anatomic relationship between the main pancreatic duct and the common bile duct has been repeatedly studied as a possible explanation for pancreatitis and its sequelae. These ducts merge above a common sphincter in over 60 per cent of persons (Mehnan; Rienhoff and Pickrell). A more important question, the length of the ampulla compared with the diameter of the common orifice, finds little agreement (Cameron and Noble; Judd; Mann and Giordano; Rienhoff and Pickrell). The fact remains that in a certain number of persons an obstruction at the ampulla of Vater might result in passage of bile into the main pancreatic duct, followed by edema, increased intraductile pressure, breakdown of alveolar elements and pancreatitis. Thus a degenerative

cyst (pseudocyst) may develop as the direct result of inflammation of the pancreas and as the indirect result of an anatomic configuration of the duct systems.

The role of pancreatitis as the chief etiologic agent responsible for the development of pseudocyst has received considerable support (Mahorner and Mattson; Pinkham). Certainly the large, encapsulated, rapidly developing peripancreatic collection containing hemorrhagic fluid, necrotic fat, cellular debris and bits of pancreatic slough cannot be regarded as other than the result of an acute necrotizing pancreatitis. The smaller cystic accumulations, lying within the gland substance or at the periphery and containing clear, mucoid or somewhat turbid fluid, obviously result from a less severe initial process. Recurrent pancreatic edema associated with spasm of the sphincter of Oddi is a suggested cause (Archibald and Kaufmann), but why should one localized area become the site of cystic change? Obstructive metaplasia of the epithelium of smaller ducts has been described (Rich and Duff), which might logically explain a localized inflammation, with acinar coalescence and subsequent degeneration.

The frequency with which demonstrable disease of the biliary tract has been found associated with pancreatitis and degenerative cyst is well known (Archibald and Kaufmann; Judd; Judd, Mattson and Mahorner; Opie; Pinkham). That this association is on a basis of infection is borne out by the fact that in most cases the main pancreatic duct is not obstructed.

The third etiologic factor, trauma, is difficult to evaluate. A history of injury preceding the appearance of a mass in the upper abdominal region is stated to be present in about 20 per cent of cases (Case; Pinkham), but an average of six reported groups (Adams and Nishijima; Judd; Mahorner and Mattson; McWhorter; Rabinovitch and Pines; Takaysu) yields 9.8 per cent. Insistent questioning may lead to unwarranted assumption by the patient and the physician that some trauma sustained in the past is directly responsible for the present illness. However, in certain cases the history of trauma of the upper abdominal region followed within a short time by an enlarging epigastric mass is too definite to be discarded.

The pancreas is soft and relatively flattened and overlies an unyielding vertebral column. A severe blow could conceivably result in a "bursting" of acinar cell groups and destruction of tissue due to enzyme activity, with slow or rapid accumulation of fluid. However, gross traumatic rupture of the pancreas is less common than similar injury of the spleen or liver. It is suggested that when trauma does play a part in the development of degenerative pancreatic cyst, it does so by means



of its effect on a pancreas whose duct system is imperfectly developed embryologically or on a pancreas which is already the seat of a subacute or chronic inflammatory process.

#### SYMPTOMS AND SIGNS

Pain is the most constant symptom (Adams and Nishijima; Case; Rabinovitch and Pines) reported present in 85 per cent of cases in which no lesion other than the cyst could be held accountable (Judd, Mattson and Mahorner). It is commonly felt in the epigastric and left hypochondriac regions, may radiate to the back, particularly on the left side, and varies in description from a dull ache to an incapacitating colic. The dragging weight of the cyst fluid probably contributes as much discomfort as does the pressure exerted on surrounding organs. Association with intake of food is not usually definite. While the onset may appear to have been sudden in nature, careful questioning may elicit a history of previous milder transitory attacks, often antedating the acute episode by several weeks or months (Rabinovitch and Pines). In some cases there is an insidious beginning, with a history of epigastric fulness, "bloating" or "indigestion" preceding specific pain.

Loss of weight (Benson and Gordon; Case; Judd, Mattson and Mahorner; Rabinovitch and Pines) and weakness (Case; Judd, Mattson and Mahorner) are common complaints. Jaundice is reported in from 7 (Korte) to 18 (Rabinovitch and Pines) per cent of cases and may be due to coexisting disease of the biliary tract rather than to extrinsic pressure by the cyst on the common duct. Nausea and vomiting are mentioned as common (Judd and others; Rabinovitch and Pines) and rare (Case). Foamy, fatty stools, characteristic of cystic fibrosis of the pancreas in children (Kennedy), are not usual in adults.

A palpable mass in the upper abdominal region is the most constant single diagnostic sign (Adams and Nishijima; Bowers and others), detectable in about 95 per cent of cases (Benson and Gordon; Judd and others; Korte). The mass is tense, rounded, relatively nontender, most often in the midline (Korte) or slightly to the left of the midline (Judd and others) in location, and is not particularly movable unless originating in the tail of the gland, when movability in the long axis of the body may be a feature (Benson and Gordon). It may develop rapidly (Case; Takaysu), there may be a long period of gradual increase in size (Benson and Gordon) or a mass known to have been present for some time may suddenly enlarge (Carter and Slattery). Fluctuation in size may be noted (Judd and others), and occasionally a cyst may disappear clinically altogether (Case), presumably when spontaneous drainage occurs into the intestinal tract.

## DIAGNOSIS

Consideration of the diagnosis of cyst of the pancreas should be included in a given case on the basis of a palpable mass in the upper abdominal region in or near the midline, coupled with symptoms of pain, loss of weight, weakness and nausea and vomiting. When a pancreatic cyst becomes large enough to produce symptoms, it is also usually large enough to produce a rather typical roentgenographic defect by extrinsic pressure on surrounding organs. Much reliance must therefore be placed on barium examination of the upper gastrointestinal tract. Excellent papers by Case and Borak have emphasized the following roentgen features of diagnostic importance:

1. An extensive, palpable tumor is most likely extrinsic to the stomach.

2. Widening of the duodenal curve is significant of enlargement in the region of the pancreatic head. Exceptions may occur when obesity is present, in cases of relaxed diaphragm with high stomach and in the presence of ascites.

3. Increase in the distance between the vertebral column and the stomach may be apparent in the lateral view.

4. There may be constant filling of the duodenum, which normally is rapidly filled and rhythmically emptied and therefore demonstrable for only short periods.

5. The left side of the diaphragm may be elevated and may show diminished excursion.

6. In the more obese patient a plain roentgenogram of the abdomen may reveal a shadow which by position and relationship to other organs may be identified as a new growth of pancreas.

7. Growths of the pancreatic head usually do not displace the duodenum forward, since both pancreas and duodenum are situated at the same level. (A rare exception to this may occur when a growth or cyst arises in the extreme lateral [right] portion of the head, in which case the first part of the duodenal loop may be displaced medially and anteriorly.)

8. In cysts displacing the lesser curvature of the stomach, the defective shadow has a smooth contour, with the concavity toward the tumor and the edges of the gastric shadow indistinct. Uninterrupted peristaltic waves passing over a suspicious filling defect signify an extrinsic lesion. On application of pressure over the mass or change in position of the patient, the defect alters in shape or disappears.

9. When the cyst originates in the tail of the gland, there is a filling defect of the greater curvature when the patient is prone, with displacement of the greater curvature upward and to the right. This disappears

or alters in shape when the patient stands up. In addition, there may be displacement of the duodenojejunal angle downward, with compression stasis of the third part of the duodenum and poor visualization of the first loop of the jejunum. If the cyst is large, one may see compression and downward displacement of the proximal loop of the splenic flexure of the colon after a barium enema.

10. Calcification of a pancreatic cyst is occasionally seen (McCullough and Sutherland).

Case pertinently stated: "Even when it seems clearly not a lesion of the digestive tube, the roentgen visualization and study of the alimentary tract as a whole may throw important light on the identity of the tumor in question."

Laboratory studies are not of specific aid in establishing the diagnosis. Sustained increase of the blood serum amylase, probably on the basis of associated pancreatitis, may be suggestive of degenerative cyst formation (Pinkham) or of intra-abdominal rupture of cyst (Koucky and others). The serum lipase may exhibit abnormality (Johnson and Lee). While the presence of trypsin (Boyd) or of a markedly increased amylase level (Pinkham) in the fluid content of the cyst strongly suggests pancreatic origin, the detection of starch-splitting enzymes is not held to be positive proof (Boyd; Judd and others; Mahorner and Mattson; Rabinovitch and Pines).

Differential diagnosis should include cyst of the omentum, hydrops of the gallbladder, hydronephrosis, ovarian cyst, cysts or tumors of the liver (Adams and Nishijima; Case; Judd and others); retroperitoneal tumors (Adams and Nishijima; Borak; Judd and others); aortic aneurysm (Borak; Case; Judd and others); mesenteric cyst (Adams and Nishijima) splenic or adrenal tumor or cyst and cysts of the posterior gastric wall (Case; Judd and others) and tumor of the kidney or perinephritic abscess (Ormond and others).

In addition to a history which may suggest disease of the upper part of the gastrointestinal tract, elements in determining the origin of an abdominal mass are its location, size, shape and character, the relationship to surrounding structures on physical examination and roentgenologic studies, signs of disease referable to a specific organ and the presence or absence of movability, tenderness and pulsation. Tumors and cysts arising from retroperitoneal tissues in the pancreatic region or from the left adrenal and cysts of the posterior gastric wall may defy preoperative distinction from pancreatic cyst.

#### TREATMENT

Complete excision of a pancreatic cyst is the method of choice (Benson and Gordon; Carter and Slattery; Neef and others), but the procedure is possible in only a few cases (Judd and others). Attempted

excision ending in failure carries a 55 per cent mortality (Lahey and Lium). It is successfully accomplished more frequently for cystadenoma (Benson and Gordon) and for the rare dermoid cyst (DeCourcy). It may be anatomically and technically impossible to excise completely the large degenerative cyst (pseudocyst), the anterior wall of which may be composed solely of thin peritoneum of the omental bursa (Held; Pinkham), with a large base blending into most of the pancreatic substance without demarcation of the posterior cyst wall.

Enucleation of a cyst confined to the head of the pancreas presents the problem of injury to the duct of Wirsung or to the accessory duct of Santorini (Lahey and Lium), and fistula formation may occur (Benson and Gordon). The proximity of the common bile duct and the inferior vena cava and the renal veins posteriorly are definite hazards. The serosa of the duodenal loop may blend with the cyst wall after inflammatory reaction, making dissection difficult. Rarely, a cyst located in the pancreatic head may be so masked by associated chronic pancreatitis, with enlargement and hardness to palpation, that an erroneous impression of carcinoma may lead to unnecessary pancreatoduodenectomy (Carter and Slattery).

In cases of cysts of the body and tail of the gland the splenic vein, left renal vein and origin of the superior mesenteric artery may be subjected to surgical trauma. Intimate relationship between splenic vein and cyst wall is not uncommon (Bowers and others). Unusual vascularity of the cyst wall itself may be a feature (Carter and Slattery) prohibiting excision (Babcock and others). When the cyst arises in the tail of the gland the pedicle is often narrow, extirpation is easier and damage to the gland substance is more easily repaired.

Previous external surgical drainage is no bar to attempted excision, success having recently been reported in a case in which eight previous drainages had been done (Carter and Slattery).

If surgical excision is impossible or inadvisable, treatment along lines of internal or external drainage may be carried out. Simple puncture and aspiration of cyst fluid may occasionally give good results (Martin) but is not to be recommended. Lahey favors primary anastomosis between cyst and gastrointestinal tract, and a loop of jejunum would appear to be the site of choice (Adams and Nishijima; Chapman; Chesterman; Hahn). If anastomosis is made between cyst and stomach, it is possible that pancreatic enzymes may in time alter the gastric mucosa, leading to pernicious anemia (Altshuler and Meyers). Physiologically, the gallbladder would seem less desirable than the jejunum and by its relatively fixed position might interfere with subsequent shrinkage of the cyst wall. Internal anastomosis is feasible when the

cyst is solitary and when its wall is of sufficient thickness and quality to withstand suturing. It is contraindicated in cases of multiloculated cystadenoma.

External drainage (Johnson and Lee; Pinkham) or marsupialization followed by treatment of the cyst cavity with sclerosing solutions (Walker) may give good results in cases of degenerative cysts, and the majority of the resulting external fistulas heal spontaneously (Lahey and Lium). However, in certain instances persistent discharge may become a prolonged and troublesome complication (Judd and others; Kerr), and if the fistulous tract heals superficially, there may be subsequent reaccumulation of cyst fluid, which necessitates additional drainage (Carter and Slattery; Mahorner and Mattson; Pinkham). The chronic fistulous tract which refuses to heal after a thorough trial of conservative measures should be transplanted into the jejunum. The mortality for this procedure in competent hands is 3.8 per cent (Lahey and Lium). Roentgenologic visualization of the tract by means of injection of iodized poppyseed oil 40 per cent is a worth while step (Borak), since communication with the main pancreatic duct may preclude healing without transplantation (Lahey and Lium).

Pancreatic cyst of the pseudocyst variety will occasionally perforate into the general peritoneal cavity either spontaneously or after trauma (Koucky and others). The findings are those of perforative peritonitis, and after shock has been combated immediate operation, with marsupialization, is indicated. A cyst has been known to perforate into an adjacent organ such as the stomach, producing a bizarre picture (Pascucci).

Diabetes, usually mild, may accompany cystic disease of the pancreas (Benson and Gordon; Johnson and Lee; Pinkham), occurring in about 6 per cent of cases (Judd and others).

The accompanying table reveals the following significant facts: The majority of the cysts occurred in women, a finding in agreement with other reports (Adams and Nishijima; Benson; Bowers and others; Held; Johnson and Lee; Rabinovitch and Pines). The average age was 48.5 years. Major symptoms in order of their frequency were abdominal pain, loss of weight, nausea and vomiting, "gas," loss of appetite, aversion to fatty foods and sense of fulness. In 6 patients the acute phase of the illness preceding the initial operation averaged 7.2 weeks. Four gave no history of similar previous attacks of abdominal discomfort or digestive difficulty. In none was there a recorded history of trauma. In every case there was a palpable mass. Six were classified as degenerative cysts (pseudocysts) and 2 as multilocular pseudomucinous cystadenomas. In 5 cases the cysts were so large and the pancreas so completely involved that the exact site of origin in the gland could not be determined.

*Data on Patients with Pancreatic Cysts*

Case	Sex	Age	Principal Symptoms	Duration of Present Illness	History of Previous Attacks	History of Trauma	Abdominal Signs	Preoperative Diagnosis	Operative Findings	Operative Treatment	Complications
1	M	55	Epigastric pain, nausea and vomiting, weight loss (17 lb. [7.7 Kg.]), "gas," fullness and weakness	3 mo.	None	None	Epigastric mass fixed, barely palpable	Carcinoma of stomach	Solitary cyst size of orange in head of pancreas; biliary tract normal	Excision	None
2	F	64	Epigastric pain and soreness; "gas" after meals	1 mo.	None	None	Nontender mass size of grapefruit extending to umbilicus	Abdominal mass of undetermined origin	Cystic pancreas; dark fluid and slough	Drained (5 cigaret drains)	Drained 6 wk.; spontaneous closure
3	F	56	Nausea and vomiting, anorexia and weight loss (26 lb. [11.8 Kg.])	4 mo.	None	None	Smooth, nontender mass extending below umbilicus, slightly movable	Retropititoneal tumor or pancreatic tumor	Cyst, sloughing pancreas	Marsupialization (cigaret drains)	Drained 9 mo.; spontaneous closure
4	M	31	Pain in left lumbar region for one week followed by epigastric pain for one week	2 wk.	None	None	Large firm mass in upper region of abdomen	Abdominal mass of undetermined origin	Multilocular pseudomucinous cystadenoma	Excision (partial)	Redrainage in 2 and 7 mo.
5	F	50	Pain in upper abdominal area, nausea and vomiting, jaundice and weight loss (amount unknown)	Several weeks	Cholecystectomy and appendectomy 5 yr. prior to this illness	None	Ascites; liver enlarged; tender mass in left upper quadrant	Biliary cirrhosis; common duct obstruction due to stone or tumor; toxic hepatitis and splenitis	(Postmortem) Carcinoma of head of pancreas with metastasis to liver, lungs; large multilocular pseudo-mucinous cystadenoma of tail of pancreas	Died 11 days after admission; no operation performed	Death due to widespread carcinoma
6	F	40	Abdominal discomfort, vomiting, dyspnea and enlarging abdominal mass	Acute phase, 6 wk.	Vague pain, fullness and occasional vomiting for 12 mo.	None	Large, firm, smooth mass extending down to brim of pelvis on right	Abdominal mass of undetermined origin	Huge cyst filling most of abdomen containing 8,000 to 10,000 cc. brownish yellow fluid	Drained (1 rubber tube)	Redrainage in 1, 13 and 16 mo.; died of adenocarcinoma
7	M	52	Epigastric pain, nausea and "gas," anorexia, weight loss (30 lb. [9.1 Kg.]) and aversion to fats	Acute phase, 4 wk.	Similar attack 13 mo. ago lasting 2 days	None	Slight tenderness in epigastrium; "liver" enlarged 5 fingerbreadths below costal margin	Cystic abdominal tumor of undetermined origin	Cyst containing 800 cc. brownish, thin fluid and gangrenous mass	Removal of slough; cyst packed with gauze	Draining 48 days after operation; no further follow-up obtained
8	F	40	Epigastric pain, "gas," weight loss (22 lb. [10 Kg.]) and aversion to fats	2 yr.	Intermittent epigastric pains after meals for 3 yr.	None	Slightly tender epigastric mass to left of midline	Carcinoma of stomach; cholecystitis; gastritis; duodenitis; pancreatitis	Cyst in tail of pancreas containing 180 cc. of fluid	Evacuated; packed	Redrainage in 2½ mo. and 5 yr.; has drained continuously for past 6½ yr.

Five living patients were personally contacted at intervals varying from one to twelve years after the original operation. Four classified their general health as good and 1 as fair. All have been relieved of their original symptoms. Of four postoperative fistulas, three closed spontaneously and have remained closed for the past three years. The patient in case 8 is a candidate for transplantation of the fistulous tract into the jejunum, since after six and one-half years of constant drainage there is little likelihood of spontaneous closure.

#### REPORT OF A CASE

J. H., a 55 year old Negro, was admitted to Mercy Hospital on Dec. 8, 1946, with the chief complaints of pain in the upper part of the abdomen, nausea and vomiting, loss of weight and fatigue. Except for influenza in 1918, measles in 1922 and an operation for an inguinal hernia in 1926, he had been in excellent health and had worked as a bricklayer's helper in a local steel mill for nineteen years.

His appetite and digestion had been good all his life, such delicacies as pork chops, pigs feet, chicken neck bones and turnip greens being especially relished. During the midsummer of 1946 he noticed occasional "gas and belching," and in September there was a feeling of fullness after some meals, which was not constant and did not seem to depend on the quantity eaten.

Pain first became manifest late in September. It was located high in the epigastrium and was gnawing in character, with intervals of wavelike colic followed by periods of freedom for two or three days. The pain had no constant relationship to intake of food. At times it was severe enough to "double him up," and it gradually increased in both frequency and severity. He vomited four times during the month prior to his admission, each instance occurring several hours after the previous meal or early in the morning. No food was regurgitated, the vomited material consisting of a small amount of bitter, light brown "juice." His appetite remained good throughout the entire illness. His bowels moved regularly each day, the stools being of solid consistency and brown. Over a period of ten weeks there had been progressive weakness and easy fatigue, with a weight loss of 20 pounds (9.1 Kg.). The remainder of the patient's history was noncontributory.

Physical examination revealed a thin, rather undernourished Negro who appeared chronically ill. Other than borderline hypertension (blood pressure 146 systolic and 90 diastolic), the only remarkable physical finding was a firm, non-tender, barely palpable mass lying deep to the midline of the epigastrium and slightly to the right. Its exact size could not be determined with accuracy.

Laboratory studies revealed a red blood cell count of 4,010,000, a hemoglobin content of 78 per cent and a white blood cell count of 7,900. The urine was normal. The phenolsulfonphthalein test showed 65 per cent excretion. The Wassermann reaction was negative. The nonprotein nitrogen was 24.7 mg. and the urea nitrogen 10.2 mg. The prothrombin time was 100 per cent.

Roentgenologic observations of the upper part of the gastrointestinal tract were reported as follows: "The esophagus is normal. There is an ulcerating carcinoma involving the pyloric third of the stomach. There is a palpable mass in relation to the lesion. The lesion appears operable."

On Dec. 13, 1946, the patient's abdomen was opened under spinal anesthesia. The gallbladder, liver, spleen and transverse colon were normal on inspection and palpation. Situated in the head of the pancreas was a rounded, tense, cystic mass of an estimated diameter of 10 cm. It appeared to have originated in the most lateral part of the pancreatic head, since the proximal portion of the duodenal loop was displaced medially and anteriorly, with the serosa intimately adherent to the cyst wall. The pyloric and prepyloric areas of the stomach were pushed upward. After evacuation of the clear, watery content, dissection and removal of the entire cyst wall was possible. During this process no large pancreatic duct was observed, but the common bile duct was inadvertently nicked, necessitating T tube drainage. Bleeding points in the head of the pancreas were controlled with suture and with gelfoam® (absorbable gelatin sponge) and thrombin. Palpation of the stomach failed to reveal an intrinsic mass. The abdomen was closed in layers without drainage other than the tube in the common duct.

Microscopic sections of the cyst wall showed chronic inflammation. There was no epithelial lining.

On the fifth postoperative day the tube in the common duct was dislodged accidentally by the patient and had to be removed. Copious bile-stained drainage gradually diminished, and it ceased on the fourteenth postoperative day. At no time did the drainage cause irritation of the skin. The wound healed primarily, and the patient made an uneventful recovery.

Follow-up studies revealed a negative van den Bergh reaction, a blood sugar content of 107 mg., glucose tolerance fasting 96, 45 minutes 176, two hours 130. The urine reacted negatively to the test for sugar. Roentgenologic study of the upper part of the gastrointestinal tract twenty days after operation revealed: "The pyloric deformity previously described, which had the appearance of a carcinomatous mass in the stomach, has now disappeared. Peristaltic movements and mucosal pattern appear relatively normal throughout the pyloric end of the stomach. The findings are now compatible with the operative diagnosis of pancreatic cyst which previously caused the deformity, and after removal the stomach has resumed normal appearance and function."

The last examination, one year postoperatively, found the patient in good health, with normal appetite and no digestive discomfort. He had gained 26 pounds (11.8 Kg.) and was working regularly in the steel mill.

#### COMMENT

This case is reported in detail in order to emphasize the fact that a cyst located in the pancreatic head can produce a clinical and roentgenologic picture closely simulating primary neoplasm of the stomach. The insidious onset of mild digestive discomfort, followed later by pain, nausea and vomiting, weakness, fatigue and loss of weight, with the presence of a deeply situated, barely palpable mass in the upper abdominal region, might suggest a malignant process. A persistently good appetite, however, is not so common in malignant conditions of the stomach, nor is vomiting without relation to intake of food.

The roentgenologic findings in this case are of particular interest. In the preoperative roentgenograms (fig. 2A) there is a constant filling defect in the prepyloric region, at the lesser curvature. This



deformity could not be displaced or made to disappear by palpation or by change of the patient's position during fluoroscopy. There is no marked widening of the duodenal loop and no smooth concavity within this loop. Instead, there is anterior and medial displacement of the first and second portions of the duodenum. Some stasis or "puddling" is evident in the descending duodenal limb. For comparison, figure 2 *B* reveals the condition of the upper gastrointestinal tract twenty days after excision of the cyst. The prepyloric region of the stomach now shows normal filling and mucosal pattern. The first portion of the duodenum has assumed a more normal appearance and position. The stasis of the descending duodenal limb has been relieved.

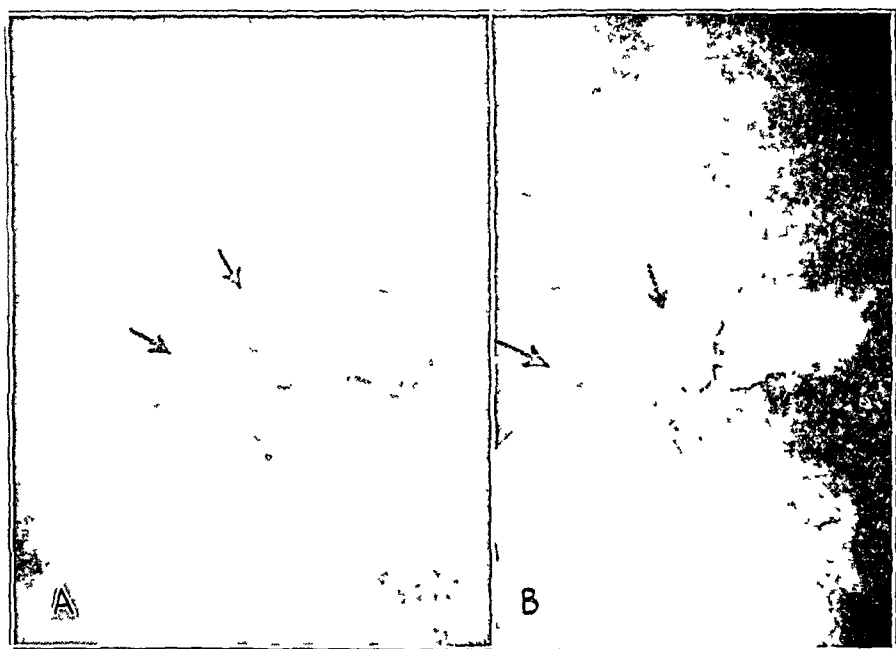


Fig. 2—*A*, preoperative roentgenogram of stomach showing prepyloric deformity (upper arrow) and location of cyst (lower arrow), with medial and anterior displacement of the first and second portions of the duodenum. *B*, roentgenogram of stomach twenty days after removal of cyst in head of pancreas. Prepyloric defect has disappeared (upper arrow), and the beginning of the duodenal loop has assumed a more normal outline and position (lower arrow).

#### SUMMARY AND CONCLUSION

1. The salient features of pancreatic cyst are discussed according to classification, anatomy and presentation, etiology, symptoms and signs, diagnosis, surgical treatment and complications. Attention is devoted chiefly to degenerative cyst (pseudocyst).

2. Findings from 8 cases are presented in brief. In 6 the tumors were of the degenerative type, and in 2 they were pseudomucinous cystadenomas. The follow-up status of 5 living patients is included.

3. One of the 8 cases is presented in detail, since the findings clinically and roentgenographically simulated those in cases of neoplasm of the stomach, leading to erroneous preoperative diagnosis. The cyst originated in the lateral margin of the pancreatic head, producing an unusual medial and anterior displacement of the first and second portions of the duodenal loop and a constant prepyloric gastric deformity.

Epigastric pain and a palpable mass in the upper abdominal region are characteristic of pancreatic cyst. Roentgenologic findings are usually confirmatory of an extrinsic gastric lesion. Occasionally, preoperative differentiation from carcinoma of the stomach may be impossible.

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# NECROSIS OF THE LIVER PRODUCED BY THE COMBINATION OF EXPERIMENTAL HYPERTHYROIDISM AND INFLAMMATION

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IN THE study of the effects of long-standing clinical hyperthyroidism, it has been noted that certain abnormalities of the liver occur. These changes are a decrease in function<sup>1</sup> and, occasionally, alterations in the structure of the liver.<sup>2</sup> The latter manifestation is not frequent, as shown by a recent report from the Massachusetts General Hospital,<sup>3</sup> where no evidence of marked hepatic damage was found in any of the autopsy cases of human hyperthyroidism studied. In the group of 11 cases previously reported from this clinic, severe changes in the liver were seen in only 2.<sup>4</sup>

In investigating this problem in the laboratory, it was noted that experimental hyperthyroidism induced in rabbits with desiccated thyroid produced profound inanition and death without significant alterations in the hepatic structure.<sup>5</sup> On the other hand, if this were complicated by infection, severe changes in the liver resulted.<sup>6</sup> Similar

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3. McArthur, J. W.; Rawson, R. W.; Means, J. H., and Cope, O.: Thyroid Crisis, *J. A. M. A.* **134**:868-874 (July) 1947.

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6. Haban, G.: Leberveränderungen bei experimentellem Hyperthyroidismus, *Beitr. z. path. Anat. u. z. allg. Path.* **95**:579-580 (Sept.) 1935.

findings were obtained by Haban, while McIver<sup>7</sup> showed that in hyperthyroid rats both small doses of chloroform and a low oxygen environment would result in necrosis of the liver. Then it was evident that hyperthyroidism in some way interfered with the normal function of the liver, leaving this structure prone to injury from agents that in the normal animal are tolerated without noticeable anatomic change in it.

TABLE 1.—*Group I. Normal Rabbits Receiving Desiccated Thyroid*

	Days and Amount of Desiccated Thyroid, Gm	Loss of Weight, Gm.	Survival in Days	Changes in the Liver
3.....	5 0.512	500	6	0
4.....	8 0.512	650	6	0
5.....	9 0.512	725	7	0
6.....	8 0.512	1,025	7	0
7....	9 0.512	500	10	0
8.....	5 0.512	500	6	0
15.....	3 0.512	250	4	0
237....	21 0.512	825	22	0
238.....	33 0.128	600	34	0
239.....	11 0.768	775	11	0
401....	6 0.768	400	7	0
403.....	15 0.768	675	15	0
404.....	6 0.768	325	7	0
406.....	6 0.768	725	7	0
409.....	13 0.768	475	13	0

If, then, infection with virulent hemolytic *Staphylococcus aureus* results in necrosis of the liver in the hyperthyroid rabbit, it was of interest to know just what factor in infection was capable of causing this change. This then would give information as to the effect of tissue necrosis, bacterial toxins or bacteria on the animal.

7. (a) McIver, M. A.: Increased Susceptibility to Chloroform Poisoning Produced in the Albino Rat by Injection of Crystalline Thyroxine, *Proc. Soc. Exper. Biol. Med.* **45**:201-206 (Oct.) 1940. (b) McIver, M. A., and Winter, E. A.: Deleterious Effects of Anoxia on the Liver of the Hyperthyroid Animal, *Arch. Surg.* **46**:171-185 (Feb.) 1943.

Desiccated thyroid is prepared from beef thyroid and is capable of increasing the metabolism of an animal just as thyroxin. Its action is thought to increase only the oxidation of the cell and is not cytotoxic in any other manner.

To study the effect of the various factors in infection that might result in necrosis of the liver, the toxin of hemolytic *Staphylococcus aureus* was used. This is a potent bacterial substance and when given intravenously in small amounts causes death immediately. If the toxin

TABLE 2.—Group II. Normal Rabbits Receiving *Staphylococcus Toxin* Subcutaneously

Rabbit	Number of Subcutaneous Injections, Amount and Reaction	Loss of Weight, Gm.	Survival in Days	Changes in Liver	Changes in Kidney
28.....	15 0.5 cc. ++++	450	16	0	0
29.....	4 0.5 cc. ++++	450	5	0	0
35.....	8 0.5 cc. ++++	400	8	0	0
4C.....	6 0.5 cc. +++	350	7	0	0
8C.....	16 0.25 cc. +++	50	17*	0	0
16C.....	5 0.25 cc. ++	200	6	0	0
18C.....	7 0.25 cc. ++	50	8*	0	0
19C.....	7 0.25 cc. ++++	400	8	0	0
20C.....	7 0.25 cc. ++	50	8*	0	0

\* These rabbits were killed.

is diluted further and the animal allowed to survive a few hours, pronounced necrotizing tubular and glomerular changes in the kidneys occur.<sup>8</sup> When the smaller doses are given, the animal may survive, and the renal lesions will eventually heal. The liver, except for occasional areas of fatty infiltration and hemorrhage, is not involved in this process.<sup>8</sup>

When *staphylococcus* toxin is injected subcutaneously, widespread local necrosis of the skin occurs. The effect on the animal of a single injection, other than a local change, is not marked. The injections can

8. Rigdon, R. H.: Some of the Experimental Lesions Produced by *Staphylococcus Toxin*, South. M. J. 32:798-802 (Aug.) 1939.

be repeated daily until the animal succumbs from the severe sterile necrosis of the subcutaneous tissue.

In this experiment normal stock rabbits of 1,800 to 2,500 Gm., fed on a balanced ration, were divided into five groups. Group I was composed of normal rabbits given 0.512 to 0.768 Gm. of desiccated thyroid per day until death ensued (table 1). The steady loss of weight was the only important change observed in the animals before death.

TABLE 3.—Group III. *Hyperthyroid Rabbits Receiving Staphylococcus Toxin Subcutaneously*

Rabbit	Days and Amount of Desiccated Thyroid, Gm.	Number of Subcutaneous Injections, Amount and Reaction	Loss of Weight, Gm.	Survival in Days	Changes in Liver	Changes in Kidney
30.....	4 0.768	2 0.5 cc. ++++	425	1½	0	0
31.....	5 0.768	3 0.5 cc. ++++	325	4	++	0
32.....	4 0.768	2 0.5 cc. ++++	275	1½	0	0
34.....	6 0.536	4 0.5 cc. ++++	575	5	++++	0
37.....	4 0.536	3 0.5 cc. ++++	525	3	++++	0
38.....	4 0.768	3 0.5 cc. ++++	350	4	+++	0
39.....	4 0.536	3 0.5 cc. ++++	525	3	++++	0
40.....	4 0.536	3 0.5 cc. ++++	325	4	++++	0
2C.....	4 0.768	3 0.5 cc. ++++	450	4	++++	0

In group II were rabbits that were given only daily subcutaneous injections of potent hemolytic Staph. aureus toxin supplied by the Lederle Laboratories (table 2). The animals received 0.25 to 0.5 cc. of this toxin in the subcutaneous tissue of the back. This produced a severe diffuse inflammatory reaction in the subcutaneous tissue that involved the skin of the back and abdomen. Repeated injections caused massive necrosis, with mummification of the abdominal skin. Eventually death occurred in most animals, apparently from the massive necrosis in the subcutaneous tissue.

In group III were normal rabbits given desiccated thyroid, and then forty-eight hours later subcutaneous injections of staphylococcus toxin was started as in group II (table 3).

TABLE 4.—Group IV. *Hyperthyroid Rabbits Receiving Staphylococcus Toxin Intravenously*

Rabbit	Days and Amount of Desiccated Thyroid, Gm.	No. of 1 Cc. Intravenous Injections of Staphylococcus Toxin Dilution	Loss of Weight, Gm.	Survival in Days	Changes in Liver	Changes in Kidney
9.....	8 0.76S	7 1:20	750	4	0	+
13.....	3 0.76S	2 1:40	320	3	0	+
14.....	19 0.76S	14 1:40	1,000	15	0	+
1B.....	4 0.76S	1 1:10	275	8 hr.	0	+++
2B.....	4 0.76S	1 1:10	250	1	0	+++
3B.....	5 0.76S	2 1:10	375	1¼	0	++++
10B.....	12 0.76S	8 1:20	1,000	8	0	+
11B.....	12 0.76S	8 1:20	800	7	0	+
13B.....	7 0.76S	3 1:10	750	4	0	+++
14B.....	10 0.76S	7 1:10	1,050	7	0	+
20B.....	4 0.76S	2 1:10	250	2	0	++

TABLE 5.—Group V. *Normal Rabbits Receiving Staphylococcus Toxin Intravenously*

Rabbit	No. of 1 Cc. Intravenous Injections of Staphylococcus Toxin Dilution	Loss of Weight, Gm.	Survival in Days	Changes in Liver	Changes in Kidney
1.....	8 1:10	0	12	0	++
11.....	9 1:20	0	10*	0	++
12.....	8 1:20	0	9*	0	+
17.....	2 1:10	0	2	0	+++
4B.....	7 1:10	0	8*	0	++
8B.....	4 1:10	0	5	0	++
16B.....	1 1:10	0	8 hr.	0	++++
17B.....	1 1:10	0	8 hr.	0	++++
18B.....	1 1:10	0	8 hr.	0	+++

\* These rabbits were killed.



Group IV was composed of normal rabbits given dilutions of *Staph. aureus* toxin intravenously that varied in concentration from 1 to 10 to 1 to 100. The dilutions were carried out in isotonic sodium chloride solution, and the injections were given immediately after preparation of the solution. The rabbits varied somewhat in their response to the toxin. A 1 to 10 dilution produced a profound toxic reaction and immediate death in about one half of the animals (table 4).

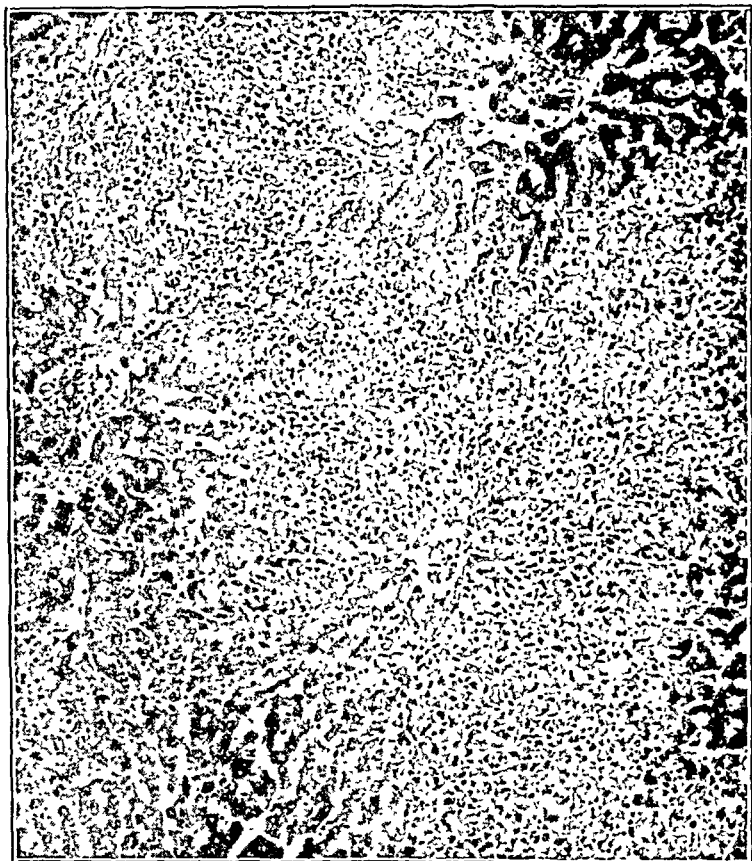


Fig. 1.—Section from the liver of rabbit no. 40 showing extensive central and focal necrosis resulting from hyperthyroidism and inflammation of the subcutaneous tissue.

Group V was composed of normal stock rabbits given desiccated thyroid by mouth forty-eight hours before intravenous injection of the toxin of hemolytic *Staph. aureus* was started just as in group IV (table 5).

Complete autopsies were done on all animals. Sections were fixed in both Zenker's solution and 10 per cent formaldehyde and subsequently stained with hematoxylin and eosin.

In group I, in which only desiccated thyroid was administered, no significant changes were produced in the liver. In group II the repeated

injections of subcutaneous staphylococcus toxin, though causing death, did not result in any morphologic changes in the liver. In group III, however, in which both toxin subcutaneously and thyroid were given, 7 of the 9 animals showed necrosis of the liver. The rabbits without change in the liver died thirty-six hours after the subcutaneous administration of toxin was begun.

The necrosis of the liver seen in group III was striking. It involved focal and central areas of the liver lobule, and caused complete disintegration of the cells in exactly the same manner as that described in

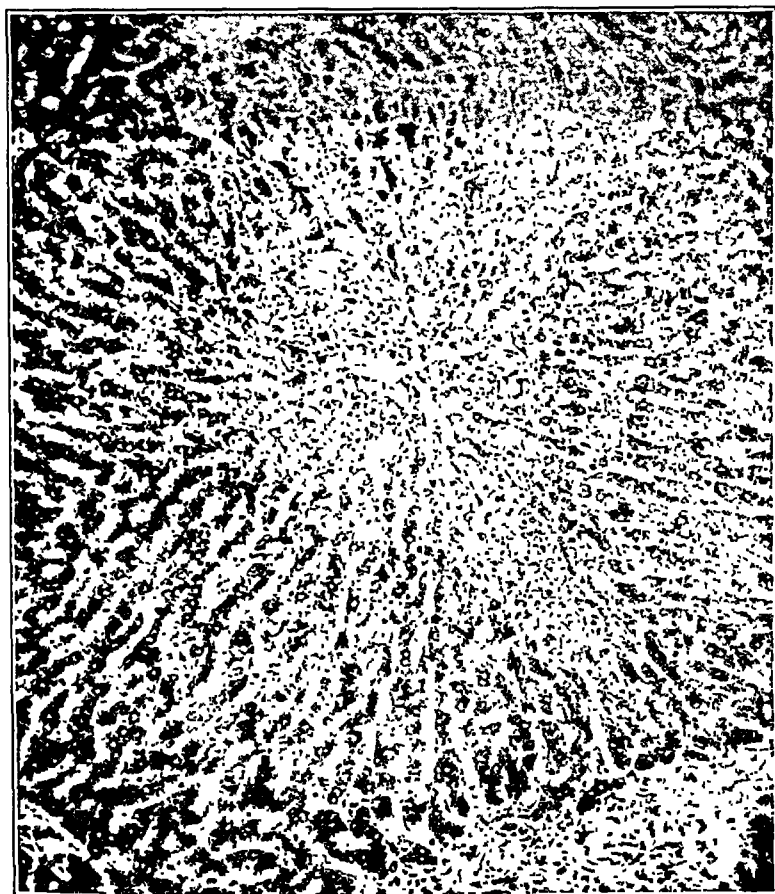


Fig. 2.—Section from the liver of rabbit no. 31 showing a small area of central necrosis resulting from hyperthyroidism and inflammation.

previous papers.<sup>9</sup> In addition, there was marked infiltration of the areas with acute inflammatory cells. Figures 1 and 2 show representative sections from this group.

In groups IV and V, in which both the animals fed thyroid and normal rabbits were given varying amounts of the staphylococcus toxin intravenously, no changes in the liver resulted. However, the typical changes in the kidneys were seen, as has been described in other reports.<sup>7b</sup>

9. Footnotes 4 and 5.

From those experiments it is evident that the toxin of hemolytic *Staph. aureus* is not capable of producing significant changes in the liver of the normal or hyperthyroid rabbit. Massive doses of desiccated thyroid alone will not produce changes in the liver. On the other hand, when massive subcutaneous inflammation and necrosis induced by staphylococcus toxin are combined with experimental hyperthyroidism, necrosis of the liver ensues.

The effect of toxic substances produced by the destruction of the animal's own tissue is not well understood. It is a common clinical observation that patients with a chronic infection or a large necrotic tumor become toxic. The reason for this progressive debilitated state is not known. It is considered that the effect of thyroxin on the liver and other cells is nonspecific, only causing a notable increase in cellular metabolism. Then perhaps the hyperthyroid animal can be used for localizing the effect of certain poorly understood toxic substances. A similar occurrence was demonstrated in the myocardium by Schultz<sup>10</sup> using streptococcic infection in hyperthyroid guinea pigs. One may postulate that the presence of necrotic tissue has a definite effect on the liver that does not manifest itself as morphologic changes in hepatic cells of animals with a normal metabolism; but in hyperthyroidism the liver is markedly vulnerable to the toxic substance elaborated by necrotic tissue.

#### CONCLUSIONS

Sterile inflammation of the subcutaneous tissue of hyperthyroid rabbits induced by staphylococcus toxin causes necrosis of the liver. The intravenous administration of staphylococcus toxin to hyperthyroid rabbits does not produce changes in the liver.

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10. Schultz, N. P.: The Induction of Carditis by the Combined Effects of Hyperthyroidism and Infection, *Pub. Health Rep.* **54**:1205-1228 (July) 1939.

# REPAIR OF ANTERIOR SUBCOSTOSTERNAL HERNIA OF THE DIAPHRAGM (HERNIA OF MORGAGNI) USING A FLAP OF TRANSVERSALIS FASCIA

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ALTHOUGH diaphragmatic hernia in general has ceased to be a rare disease, the anterior subcostosternal type (i. e., through the foramen of Morgagni) is unusual. Hedbloom<sup>1</sup> stated that about 60 poorly documented cases had been described up to 1938 in a study of 1,003 diaphragmatic hernias of all types. Harrington<sup>2</sup> pointed out that 24 instances were reported between 1930 and 1942. Only 5 patients had undergone surgical treatment. In his own series of 270 diaphragmatic hernias there were 4 of the subcostosternal type operated on. In a later article<sup>3</sup> the same author added 4 more cases of this type, which made a total of 8 in his personal experience with 404 diaphragmatic hernias.

Subcostosternal hernias or hernias through the foramen of Morgagni have been classified as congenital and acquired. As stressed by Harrington, the constant location of the hernial hiatus, the constant relation of the neck of the sac to the round and falciform ligaments of the liver and the occasional association of the condition with nonrotation of the right side of the colon all suggest an embryologic malformation. The presence of a peritoneal sac indicates that the abdominal cavity has been invested by peritoneum prior to herniation of the abdominal organs. The condition therefore occurs relatively late in fetal life.

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1. Hedbloom, C. A.: *Ann. Surg.* **94**:776-785 (Oct.) 1931.

2. Harrington, S. W.: *Surg., Gynec. & Obst.* **73**:601-614 (Nov.) 1941.

3. Harrington, S. W.: *Ann. Surg.* **122**:546-568 (Oct.) 1945.

Though probably congenital in origin, the subcostosternal hernia is found most often in later life, probably because of increased intra-abdominal pressure exerted against a congenitally weak point in the diaphragm. Donovan<sup>4</sup> reported finding the hernia in a 16 month old male infant who had symptoms at the age of 2 months and also in a 12 year old boy. The majority of instances have involved adults, with no particular sex preponderance.

In the normal person, weak areas in the diaphragm are found in the subcostosternal spaces of Larrey. These triangular spaces are bounded



Fig. 1.—Preoperative barium enema showed the transverse colon in the hernial sac.

by the sternal portion of the diaphragm medially, laterally by the costal portion of the diaphragm near the seventh costal cartilage and anteriorly by the sternum. The spaces are occupied by areolar and connective tissue with a covering of pleura and pericardium superiorly and peritoneum inferiorly. Occasionally, the sternal attachment of the diaphragm is entirely absent and the two spaces of Larrey fuse into a large defect behind the sternum and the neighboring costochondral junctions. The following case is illustrative of this type of hernia.

4. Donovan, E. J.: *Ann. Surg.* **122**:569-581 (Oct.) 1945.

## REPORT OF A CASE

H. T., a 29 year old white carpenter and World War II veteran, was admitted to the hospital on March 3, 1947, complaining of easy fatigability of one year's duration and chronic nonproductive cough of two year's duration. The patient stated that he had noted occasional pain in the right lower region of the chest. Since discharge from the Army in November 1945 he had gained 35 pounds (15.9 Kg.) and had noted fullness of the neck. He stated that he had felt borborygmi in the right side of the chest but had no other gastrointestinal symptoms.

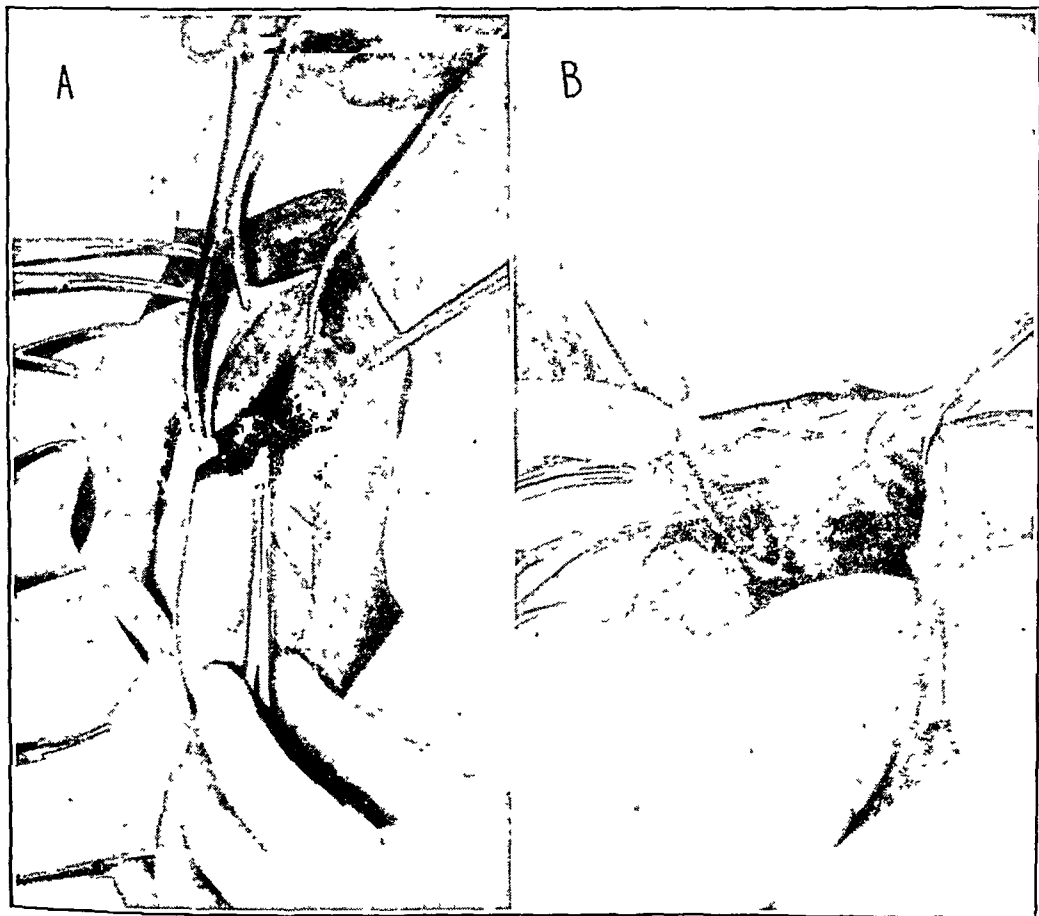


Fig. 2.—*A*, the round ligament is divided close to the liver in a cadaver. The transversus muscle flap is developed and turned back to the right. *B*, the left lobe of the liver is mobilized in a cadaver and retracted inferiorly, revealing a defect in the diaphragm.

He reported to the outpatient clinic with these complaints, where a diagnosis of hernia through the foramen of Morgagni was made after a routine roentgenogram of the chest. He was referred to the hospital. The past history was non-contributory except for surgical drainage of the right knee in 1940, which the patient thought was tuberculous.

Physical examination revealed that there was no enlargement of the thyroid. There were slight dulness and impaired transmission of breath sounds over the

lower right anterior region of the chest. Deep pressure in the right upper quadrant caused some pain in the lower right anterior part of the thorax. Examination of the right knee showed two healed operative scars.

*Laboratory and Roentgenologic Data*—Examinations of the blood and urine gave results which were within normal limits. The reaction of the blood to the Mazzini test was negative. The sedimentation rate and the basal metabolic rate were normal. The roentgenogram of the chest (fig. 1) showed an ovoid mass containing gas-filled loops of bowel lying in the lower right region of the chest anteriorly, immediately above the diaphragm and to the right of the midline. A

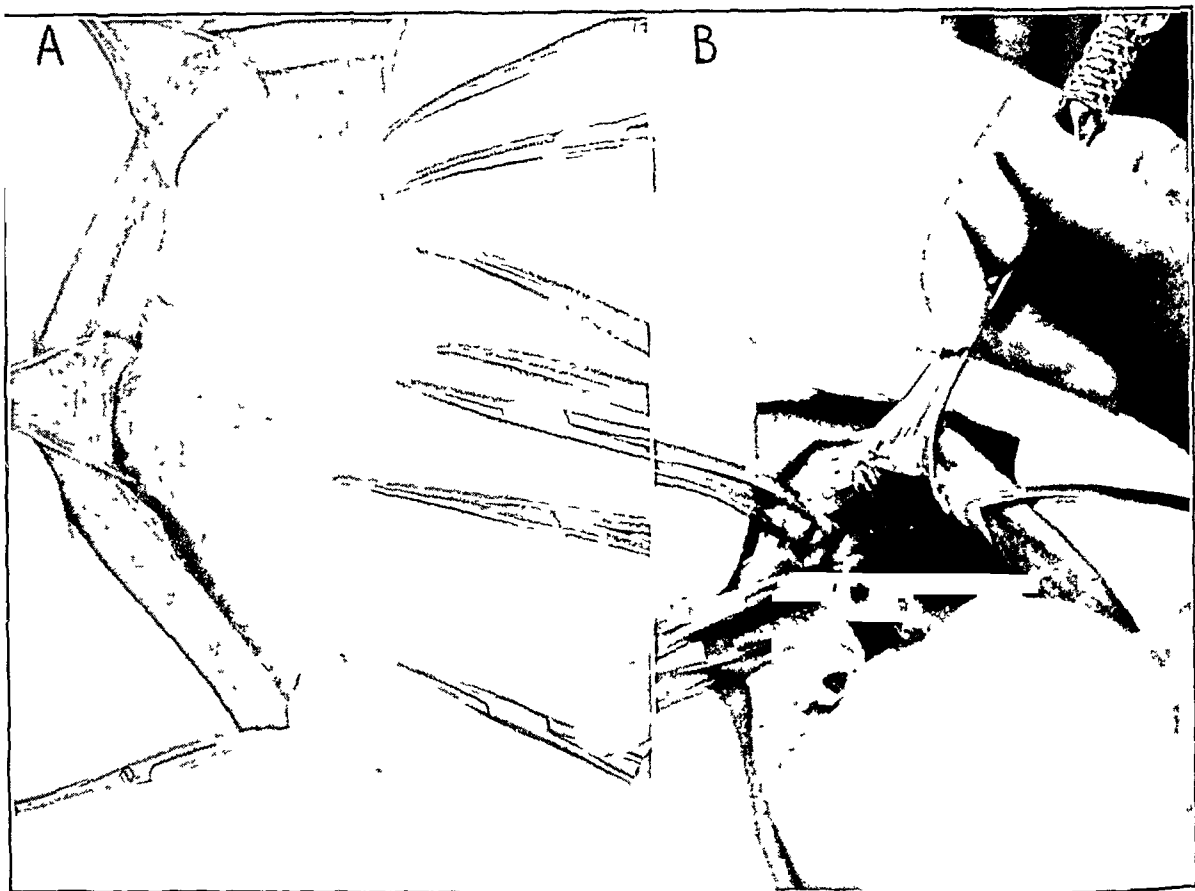


Fig. 3.—*A*, the lateral half of the right rectus muscle in a cadaver is retracted to the right, revealing the posterior sheath of the rectus and transversus muscles. *B*, The flap developed from the posterior sheath of the rectus and transversus muscles in a cadaver is swung upward and inward to effect the repair.

barium enema showed these to be loops of mid-transverse colon. A barium meal revealed no abnormality of the upper part of the gastrointestinal tract.

Exploration was performed through a right rectus incision, and a hernia in the foramen of Morgagni was found which contained a loop of transverse colon and omentum. When the viscera were reduced, the sac measured about  $3\frac{1}{2}$  inches (8.89 cm.) in depth, and its mouth measured 3 inches (7.62 cm.) transversely and  $1\frac{1}{2}$  inches (3.81 cm.) in the anterior-posterior diameter. There was no sternal attachment of the diaphragm. The round and falciform ligaments

of the liver formed the right lateral border of the mouth of the sac. The diaphragmatic defect was repaired with a sliding flap of the transversus abdominis. Because this is believed to be the first clinical application of this method, it will be described in detail.

The round and falciform ligaments were divided as close to the liver as possible and swung downward, their attachments to the abdominal wall being preserved (fig. 2A). No attempt was made to remove the peritoneal sac because of possible damage to the pericardium, which could be seen through the dome of



Fig. 4.—Postoperative barium enema showed complete reduction of the transverse colon.

the sac (fig. 2B). The peritoneum was excised from the rim of the hiatus, and the cut posterior free edge was sutured to the left leaf of the peritoneum of the anterior abdominal wall, the upper angle of the abdominal incision thus actually being closed. The right leaf of the transversus abdominis was dissected from its attachment to the xiphoid process and right costal cartilages and mobilized from the rectus muscle anteriorly and peritoneum posteriorly (fig. 3A). A flap was thus formed which was swung to the left and upward and sutured to the posterior rim of the diaphragmatic hiatus (fig. 3B). (The anterior rim was formed by the posterior surface of the sternum and the neighboring costal car-



tilages.) Since the defect was relatively small, it was possible to imbricate the flap of transversus abdominis muscle over the defect in order to reenforce the repair. The round and falciform ligaments of the liver were swung up and used to reenforce the upper angle of the closure of the peritoneum of the abdominal wall. The rest of the abdominal wall was then closed in layers. The left leaf of the transversus abdominis was sutured to the base of the flap on the right in order to close the upper angle of the muscle layer of the abdominal wall. The remaining closure was accomplished in a routine manner. Interrupted sutures of silk were used throughout. The repair was completed without tension. The patient made an uneventful recovery. A postoperative barium enema revealed a successful repair of the hernia (fig. 4).

#### COMMENT

The symptoms of hernias of this type may be mild or severe. Often they mimic those of disease of the gallbladder, pancreatitis, peptic ulcer or intestinal obstruction. Disturbances in the chest, however, are probably the most common presenting symptoms and have prompted surgeons to explore these lesions through the chest. Cough, dyspnea and precordial pain may be attributed to mechanical interference with respiration. Borborygmi in the chest may be experienced by the patient. On physical examination dulness or tympany may be elicited by percussion over the lower anterior region of the chest, depending on the absence or presence of gas-filled loops in the hernial sac. Borborygmi may be heard, and succussion sounds synchronous with the heart beat have been reported rarely.

The typical roentgenologic findings in hernias through the foramen of Morgagni have been reported by Ritvo and Peterson.<sup>5</sup> There usually is a rounded density with sharply defined borders extending from the heart shadow laterally even as far as the anterior axillary line. In the lateral view, the mass occupies the anterior and middle portions of the right lower pulmonary field and the sharp upper border blends into the shadow of the anterior wall of the chest. There may be atelectasis of the right middle lobe. The mass cannot be separated from the right border of the heart shadow, but it does not pulsate. Pericardial celomic cysts may be difficult to distinguish from a diaphragmatic hernia of this type even after careful fluoroscopy. Pneumothorax will usually help to separate the outline of the cyst from the contour of the diaphragm. If bowel loops are present in the hernia, intestinal patterns are seen which are, of course, pathognomonic. On the other hand, fluid levels may be present in the bowel which may give the erroneous impression of encapsulated pleural fluid or pulmonary abscess. The differential diagnosis between eventration of the diaphragm and hernia in the foramen of Morgagni may be difficult. However, fluoroscopic studies

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5. Ritvo, M., and Peterson, O. S., Jr.: *Am. J. Roentgenol.* **52**:399-405 (Oct.) 1944.

of the former lesion may show diminished or even paradoxical movement of the diaphragm, and oblique and lateral views will usually reveal the entire unbroken contour of the diaphragm. At any rate, pneumoperitoneum or pneumothorax will help to establish the diagnosis in most instances.<sup>6</sup> In any event, a patient with a mass in the anterior lower pulmonary field or the inferior mediastinum which is rounded and has sharply defined borders should be given a barium meal and barium enema to aid in establishing the diagnosis. At operation, usually transverse colon and omentum are found within the sac. Omentum, ascending colon, cecum, appendix and the terminal portion of the ileum have also been found. Even when the sac contains omentum alone, one may suspect subcostosternal diaphragmatic hernia because of the presence of a highly situated gas pattern in the large bowel seen in the right lateral view of the chest. Since the abdominal approach to the hernia is preferable to the thoracic approach, it is imperative to make the correct diagnosis preoperatively.

The diaphragm develops from many components, most important of which are the septum transversum which contributes the ventral portion, the pleuropericardial membranes which form the lateral segments and a median dorsal segment derived from the dorsal mesentery. In addition to these three main anlagen, the diaphragm acquires an additional rim of tissue from the abdominal wall during its development.<sup>7</sup> For purposes of discussion it is proper to consider the diaphragm as being continuous with the transversus abdominis muscle anteriorly and the lumbodorsal fascia posteriorly. Caspar Bartholin (1676) advanced such a theory, and he described the diaphragm and the transversus abdominis as a continuous muscular sheet which he called the trigastric muscle. In an excellent anatomic study Rives and Baker<sup>8</sup> recently showed that the transversus abdominis was continuous with the diaphragm at the costochondral insertion anteriorly, and they suggested the use of the former muscle in the repair of anterior defects of the diaphragm. Essentially, their method was used in the case described here.

Rives and Baker described the use of a sliding fibromuscular flap in the treatment of a large posterior diaphragmatic hernia. In their case a sliding flap was constructed from the latissimus dorsi muscle. Chisholm<sup>9</sup> in a later article described the fate of latissimus dorsi muscle flaps used to obliterate defects made in the diaphragm of a dog. The flap began to atrophy after the fifth month, and the remaining diaphragm

6. Bisgard, J. W.: *J. Thoracic Surg.* **16**:484-490 (Oct.) 1947.

7. Arey, L. B.: *Developmental Anatomy*, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

8. Rives, J. D., and Baker, D. D.: *Ann. Surg.* **115**:745-755 (May) 1942.

Rives, J. D.: *Surg., Gynec. & Obst.* **74**:1026-1028 (May) 1942.

9. Chisholm, T. C.: *J. Thoracic Surg.* **16**:200-206 (April) 1947.

stretched in order to fill in the defect. Histologic sections of the latissimus dorsi used in the flap showed early fatty degeneration and replacement fibrosis. At eleven months after operation the function of the diaphragm was unimpaired and the hernia apparently repaired.

This is the first recorded instance of the use of a fibromuscular flap in the repair of an anterior defect of the diaphragm. This operative procedure can be used to close much larger defects of the diaphragm without tension. For large defects it may be advantageous to paralyze the phrenic nerve in the neck. However, Chisholm pointed out that he was able to repair large defects in dogs without resorting to such a procedure. In effect, the technic described employs a pedicle flap of tough fascia and muscle with an intact blood and nerve supply which continues to function many months after operation. The method is especially advantageous when the retrosternal portion of the diaphragm is absent. Since the repair is an extraperitoneal one, the intestines do not interfere with the exposure. It is preferable to the use of a free graft of fascia or of fascial sutures, which have not proved universally successful.

The fact that the peritoneal sac is left behind presents no problem. A postoperative roentgenogram of the chest of this patient revealed a fluid level in the hernial sac which disappeared gradually in subsequent roentgenograms. A fluid level is of no clinical significance and should not lead one to the erroneous impression that the hernia has recurred.

#### SUMMARY

A case of diaphragmatic hernia through the foramen of Morgagni is presented. A method of repair using a flap of transversus muscle has been employed in a clinical case for the first time.

## PROGRESS IN ORTHOPEDIC SURGERY FOR 1946

A Review Prepared by an Editorial Board of the American  
Academy of Orthopaedic Surgeons

### XX. CONDITIONS INVOLVING THE SPINE AND THORAX, EXCLUSIVE OF THOSE IN THE LOWER PART OF THE BACK

Prepared by  
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#### RETRACTOR FOR SPINAL SURGERY

TAYLOR<sup>1030</sup> describes a simple retractor for spinal surgery. The advantages are derived from the principle of leverage. The important feature is a small tip, 3/8 inch wide (0.95 cm.), 1/2 inch (1.27 cm.) long and curved slightly forward at the end of the retracting blade. The tip is caught on the lateral surface of the articular facet on which leverage is made for retraction.

[ED. NOTE.—This retractor has definite advantages when the articular facets are to be arthrodesized.]

#### TREPHINEMENT

Michele and Krueger<sup>1031</sup> describe a method of trephining vertebral bodies:

A paravertebral incision is made directly over the articular facet of the vertebral body under diagnosis. The articular facet is located and the intra-articular space is gouged at a right angle, with the trephine entering into the medullary space of the pedicle. . . . The dense cortical rim of the vertebral body and of the pedicle will prevent the trephine from penetrating outside its margin. . . .

Aside from removal of the pathological tissue through the area of trephining, . . . a complete excochleation of the cancellous vertebral body can be performed with replacement by iliac graft. . . .

The question of conservative or operative treatment for spinal tuberculosis, with a beginning collapse, has thus been decided. Spinal fusion is modified by replacing pathological tissue with osteogenetic graft.

[ED. NOTE.—Any biopsy of a vertebral body is not without some danger, and it is questionable whether it should be done except in rare cases. One wonders whether it is desirable to communicate with a tuberculous abscess in front when one wishes to get a solid spinal fusion behind.]

1030. Taylor, G. M.: A Simple Retractor for Spinal Surgery, *J. Bone & Joint Surg.* **28**:183-184 (Jan.) 1946.

1031. Michele, A. A., and Krueger, F. J.: Vertebral Body Trephine: Preliminary Report, *Pub. Health Rep.* **62**:1166-1167 (Aug.) 1947.

## DISEASES OF INTERVERTEBRAL DISKS

*Rupture.*—Echols<sup>1032</sup> discusses radicular pain due to ruptured cervical disk. He classifies the several types of ruptured cervical disk according to the neural structures which they compress:

Cervical intervertebral disks which rupture into the spinal canal may produce no neurologic symptoms if the hernia is small, may merely compress a single nerve root if the nodule is small and laterally placed, may result in compression of the spinal cord and one or both adjacent nerve roots if the protrusion is large, or may compress the cord alone if the hernia is discrete and near the midline.

In reviewing the literature, the author found less than 75 reported cases of ruptured cervical disk producing compression of the cord. He points out, however, that the literature certainly does not give a true picture of the incidence, and that probably every neurosurgeon has a collection of unpublished case reports. He states:

The points of maximum pain are the base of the neck, the tip of the shoulder and the upper arm. The pain may extend into the hand and fingers but paraesthesias, including a feeling of numbness in the hand and fingers, are usually the chief complaints referable to areas below the elbow. These sensations of numbness in case of the disk below the sixth body (seventh root) are experienced chiefly in the index finger and often in the thumb and middle fingers as well. The triceps muscle may be weak and its tendon reflex may be diminished or absent. In case of the disk below the fifth body (sixth root) the numbness is slight and chiefly in the thumb and first metacarpal. The biceps muscle is weakened and its tendon reflex is decreased.

Firm pressure on the back of the neck close to the midline, says the author, may increase the radicular pain. A positive reaction to the test for foraminal compression, which consists of tilting the head toward the painful side and applying pressure on the top of the head, is almost pathognomonic. He continues:

**Seventh Cervical Disk:** Rupture of the lowest cervical disk (below the seventh body) has been reported only 10 times. . . . It may be that some of the atypical cases of scalenus anticus syndromes with pain and paresthesia in the ulnar distribution are really cases of compression of the eighth cervical root by rupture of the seventh disk.

**Sixth Cervical Disk:** The sixth cervical disk is the one which ruptures most frequently. . . . compression of the seventh cervical root . . . produces numbness and sometimes pain in the index finger and sometimes in the thumb and middle finger as well. Most of the pain is in the neck, thorax, scapula, shoulder, posterolateral surface of the upper arm, and dorsum of the forearm.

[Rupture of the fifth cervical disk] produces sensory changes chiefly in the thumb and first metacarpal region. The biceps muscle may be weak and its reflex may be absent. The pain is felt along the radial aspect of the arm and forearm.

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1032. Echols, D. H.: Radicular Pain Due to Ruptured Cervical Disk, *South. Surgeon* 12:205-218 (Oct.) 1946.

The author states that except for 3 cases listed in an article by Young, clear examples of rupture of the fourth cervical disk have not been reported. Anatomically, the pain and paresthesia should be in the neck, shoulder and arm.

Lateral rupture of the disk below the third body has not been reported. Rupture of this disk would presumably produce pain in the side of the neck and in the clavicle, supraspinatus region, and shoulder tip.

It is possible that some cases of chronic occipital neuritis are caused by a ruptured second disk. Young mentions a case of rupture of the disk below the second body which was proved by myelography and at autopsy. The patient had stiffness of the neck followed by pain in the side of the neck and elevation of the tongue, presumably because weakened infrahyoid muscles failed to fix the hyoid bone.

Roentgenologic findings are of great assistance in the differential diagnosis of pain in the neck, shoulder, and arm, but can be misleading. Probably the most constant finding . . . is loss of the normal curvature. . . . Roentgenographic evidence of narrowing of a disk is a useful finding provided it is the disk which the examiner believes, on clinical grounds, to be ruptured.

Ruptured thoracic disk will in time be considered in the differential diagnosis of chronic thoracic and abdominal pain, including the so-called intercostal neuritis.

The author reports 18 cases, recorded in a period of five years, of protruded cervical disk producing radicular syndrome, with operation in only 3. Operation was performed after conservative orthopedic measures had failed. Similar findings were reported by Elliott and Kremer, while Young reported 56 cases, in only 5 of which was surgical treatment given.

[ED. NOTE.—This is a good article; it emphasizes the importance of careful neurologic examination in cases of pain in the neck, arm and back, and the importance and efficacy of conservative treatment. It should be read in its entirety.]

*Protrusion.*—James<sup>1033</sup> discusses protruded cervical intervertebral disk as a cause of brachial neuritis. Believing that even at the time of his report the literature gave a poor idea of the incidence of this common condition, he states:

When discs protrude posteriorly the protrusion is most often laterally, as the posterior longitudinal ligament is thick in the mid-line and thinner at each side where it lies over the intervertebral disc. Mid-line protrusions do occur and may cause a paraplegia. Large lateral protrusions may compress the cord and produce a Brown-Séquard syndrome but the great majority of protrusions are farther lateral and compress the nerve root against the lamina, ligamentum flavum or articular facet. In the cervical region one damaged disc compresses one nerve root but it is possible to have more than one disc affected. . . . In the

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1033. James, E. S.: Protruded Cervical Intervertebral Discs: A Cause of Brachial Neuritis, *Canad. M. A. J.* 55:139-142 (Aug.) 1946.

lower lumbar region . . . it is possible for one protrusion to compress more than one nerve root because of their oblique descent in the spinal canal.

Most of these cases are in people past 40 years of age and no history of trauma can be obtained. Trauma, however, is a factor in young people. . . . Degeneration of connective tissue is responsible for the vast majority of cases. . . . Occasionally a history of a similar attack in the opposite arm will be obtained.

Probably all cases of the scalenus anticus syndrome are due to protruded cervical discs. [ED. NOTE.—This is probably a little too inclusive.]

Osteo-arthritis of the cervical spine has been a frequent diagnosis, suggested by the radiologist and readily accepted by the clinician. It is pointed out that the narrow disc is incidental and the nerve roots are either compressed by osteophytes or by a narrowing of the intravertebral foramina. Osteo-arthritis in the lumbar spine is not accepted as the cause of sciatica. Nature looks after her nerves and must very rarely if ever allow bony overgrowths to encroach on them. Osteo-arthritis of the spine with its lipping is a process which accompanies degeneration of the intervertebral discs.

The author reports 38 cases of lesions of a cervical disk in the past year. Myelograms were made in only a small percentage of these, and operations were performed in only 4 cases. He discusses the importance of recognizing the brachial neuritis syndrome and of appreciating the part played by the intervertebral disk and emphasizes conservative treatment.

[ED. NOTE.—The implication is that almost all instances of brachial neuritis are due to protrusion of a disk. It must be remembered that there are other causes for brachial neuritis besides protrusion of a cervical disk. Even in cases with typical signs and symptoms of protrusion of a lumbar disk, one can really only make a diagnosis of lesion of a nerve root, probably due to protruding intervertebral disk. The many other possible causes of irritation of the nerve roots can be demonstrated only at operation or in other studies.]

*General Conditions.*—Young<sup>1034</sup> also reports a study of diseases of cervical and thoracic intervertebral disks. He states the opinion that "neck pain, . . . scapular pain and . . . cervico-brachial pain" are frequently due to disease of a cervical intervertebral disk, and that whereas cervical intervertebral disks are commonly the site of degenerative processes, herniation is rare.

. . . the opposing surfaces of the cervical vertebrae are more cup-shaped than those of the lumbar region and they tend to hold the cervical disk in place.

Identical signs may occur in degeneration of a cervical disk if one vertebra suddenly subluxates on the other. Both herniation of a cervical disk and subluxation of a cervical vertebra may respond to treatment by traction, so that the final diagnosis may be made only at operation.

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1034. Young, J. H.: Cervical and Thoracic Intervertebral Disk Disease, M. J. Australia 2:833-838 (Dec. 14) 1946.

Before I knew anything about cervical disk disease I used to carry out manipulation in cases like these, sometimes producing relief. Now that I know what the pathology is and what damage may be done by manipulation, I prefer traction with a Glisson's sling.

[ED. NOTE.—This note of caution from a man of extensive experience with the problem deserves consideration by those who sometimes over-emphasize the use of manipulation.]

The author differentiates between herniation of a degenerated cervical disk and traumatic rupture of a disk followed with a later degenerative process. He states the opinion that the true incidence of disease of cervical disks is not yet known. The importance of differential diagnosis is emphasized and conservative treatment outlined. The radicular syndromes are discussed. A chart of the dermatomes and of variations in the segmental supply of the muscles and skin is included.

The author also reports a study of 66 patients with thoracic back-ache who presented no obvious evidence of visceral disease or of neurosis. He discusses the lesions in 13 cases of disease of thoracic intervertebral disks in which diagnosis was confirmed roentgenographically or at operation. Among the 4 cases in which surgical treatment was given, involvement of the third disk was noted in 1; of the tenth disk, in 2, and of the eleventh disk, in 1. In all 4 the results of the mobility test proved reliable. At the time of the report, the results were excellent. The conservative treatment of disease of a thoracic disk consists of relief of pain and avoidance of strain, with the use of a corset or brace.

[ED. NOTE.—This excellent article, by an author who has evidently had considerable experience with involvement of the disks should be read by any one interested in the problem.]

#### PYOGENIC INFECTION OF THE EPIDURAL SPACE

Rankin and Flothow<sup>1035</sup> report a case of pyogenic infection of the spinal epidural space. They state that they believe the case to be worthy of note because:

(1) There was gross radiographic evidence of osteomyelitis of the vertebrae, which is unusual in epidural granulomas; (2) the mass was situated in the cervical epidural space, where they infrequently occur; (3) the inflammatory process involved the nerve roots primarily, and there was no evidence of damage to the spinal cord itself; (4) despite inexcusable delay in carrying out the proper treatment, operation effected a complete functional recovery as well as an apparent cure of the vertebral osteomyelitis.

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1035. Rankin, R. M., and Flothow, P. G.: Pyogenic Infection of the Spinal Epidural Space, *West. J. Surg.* 54:320-323 (Aug.) 1946.



In reviewing the literature, the authors found that 217 case reports had been collected by Browder up to 1941 and that 8 cases had been reported from then to the time of the report. They stress the fact that the disease is unfamiliar to most physicians and is rarely diagnosed before the onset of irreparable damage to the spinal cord.

The disease is likely to occur in the wake of suppurative infection anywhere in the body. Since there are few physicians who are not frequently called upon to treat infectious processes it behooves us to be aware of this disease entity.

Pyogenic infection of the epidural space is not rare. It has been considered so because it is rarely recognized.

The disease occurs at any age, the youngest patient in the cases reported being an infant of 1 week and the oldest, a man of 67.

Males are affected three times more frequently than females.

Epidural space infection is always secondary to a suppurative process elsewhere in the body, although at times the primary site cannot be found. The bacteria invade the spinal canal either by direct extension from a contiguous suppuration (that is, osteomyelitis of vertebrae, sacral decubitus, or cellulitis of neck), or by metastasis via the blood or lymph channels. The latter route is exactly analogous to acute hematogenous osteomyelitis. . . . In the great majority of cases the causative organism is staphylococcus, but other organisms have been reported.

In the cervical region the [epidural] space is only a potential one but at the level of the fourth dorsal segment it broadens out and remains so down to the eighth dorsal segment where it becomes narrow, but it broadens out again between the third lumbar and the second sacral segments. It is in the broad areas that infections usually localize.

Infection in this space may be either extremely fulminating (epidural abscess) and cause death in a matter of hours, or it may be chronic (epidural granuloma) causing progressive paralysis over a period of months or years. Occasionally there occurs a subacute form made up of miliary abscesses in a fibrous granulomatous matrix. Regardless of the type of extradural infection, there is profound damage to the underlying spinal cord. Pathologically there is extensive myelomalacia with liquefaction and vacuolation of the white substance, swelling and chromatolysis of the neurocytes, and inflammatory reaction of the glial cells. The spinal cord degeneration is far out of proportion to pressure of the extradural mass itself. This is believed to be due to thrombosis of intraspinal vessels and obliteration of the intraspinal lymph spaces caused by the contiguous, but transdural, inflammatory process. There is virtually never invasion of the subarachnoid space with resultant leptomeningitis. The rare cases which have been reported have been due to: (1) osteomyelitis of the vertebral bodies bursting through the adherent dura anterior to the cord; or (2) insertion of a lumbar puncture needle through the infected area into the subarachnoid space. [ED. NOTE.—This is another situation where ill advised lumbar puncture may be a cause of considerable harm.]

The clinical course of events in epidural space infection follows a monotonously regular pattern. In the wake of any concurrent or preceding major or minor infection, the patient suddenly develops a severe intractable pain in the vertebral axis. A day or two later, or frequently within a few hours, he complains of radicular pains in the distribution of the involved segment. The vertebral and

root pains are exacerbated by coughing and sneezing. In one-half the cases there is tenderness to percussion and palpation of the involved spines, and localized swelling frequently occurs. There is marked rigidity of the spine and nuchal rigidity is present. A day or so later the inevitable symptoms of cord compression appear. There is difficulty in urination, leading to complete paralysis of the bladder. Concurrently paralysis and loss of sensation below the lesion occurs, resulting in complete paralysis and a sensory level. Beginning just prior to or at the time of the onset of the pain there is fever, which may reach high levels and is accompanied by leukocytosis, tachycardia, elevated sedimentation rate and circulatory collapse.

The spinal fluid shows quite characteristic changes. The protein is almost invariably elevated, usually 100 to 300 mg., occasionally reaching 4000 mg. There is usually, but not always, a moderate pleocytosis of 15 to 150 cells, mostly lymphocytes. Sugar and chlorides are within normal limits, but the colloidal gold curve is usually abnormal. Xanthochromia is frequent. The Queckenstedt test almost invariably demonstrates a partial or complete subarachnoid block, and on this the diagnosis is based.

In chronic and subacute epidural space infections the identical pattern and findings are present, except that the course is less fulminating and may extend over a period of months and years instead of hours or days. Also, there is little or no febrile reaction and the local vertebral signs and symptoms are less apparent.

If one is cognizant of the disease, the diagnosis may usually be inferred by the characteristic history and physical findings. Demonstration of a partial or complete subarachnoid block on the Queckenstedt test or myelography completes the diagnosis, although the inflammatory nature of the extradural mass is frequently not proven until operation is performed. In the acute form the disease is often mistaken for the other causes of acute febrile illness with localized pain: that is, pyelitis, appendicitis, pneumonia, pleurisy, and so forth. In the chronic forms it is usually confused with primary chronic neurologic diseases: poliomyelitis, multiple sclerosis, transverse myelitis, and so forth. In all cases a carefully performed Queckenstedt test should lead one to the correct diagnosis. If the physical findings make one suspicious of an epidural inflammatory mass in the lower lumbar region, puncture of the lumbar spinal sac should not be done, as a fulminating leptomeningitis may result. In these cases cisternal puncture and myelography will confirm the diagnosis. Radiographic evidence of destruction of the vertebrae themselves is the exception rather than the rule.

Once the diagnosis has been established, laminectomy is imperative. In the acute cases immediate operation is as essential as it is in cases of ruptured spleen or acute appendicitis, as irreparable damage to the spinal cord and/or death may occur in a few hours after the onset of symptoms. The mortality without operation is 100 per cent, and less than one-half of the patients whose cases are recorded were operated upon soon enough to prevent untoward results. The chronic cases are handled as any spinal cord tumor. Systemic penicillin and/or sulfonamides should always be used in conjunction with operative treatment.

The prognosis is directly proportional to the rapidity with which the diagnosis is made and proper treatment carried out. The over-all operative mortality is thirty-three and one-third per cent, most operative deaths occurring in the acute forms. Of the patients surviving operation, 40 per cent have complete return of function.

[ED. NOTE.—This is an excellent paper, reviewing the problem of pyogenic infection of the epidural space. The author has done well to bring the condition to our attention, as the diagnosis is evidently rarely made soon enough to prevent permanent disability or death.]

#### POSTURE

Kuhns<sup>1036</sup> discusses normal posture in early childhood:

Normal posture in infancy can be defined as the absence of noticeable deformity. There is no active resistance to gravity and the baby posture is molded by the contours of the furniture on which he lies. During the first year of life postural training is chiefly passive—keeping him in an environment which does not permit the long-time assumption of faulty attitudes. . . . Set exercises are rarely practicable before the school age. Posture teaching is chiefly by precept and by example. Other helpful measures such as adequate rest and proper nutrition must be kept constantly in mind.

While much of the unsteadiness and lordosis of the low back and weakness at the knee and foot are temporary and show considerable spontaneous improvement with growth, good balance of the body over the center of gravity never comes without proper development and coordinated action of the muscles which control the pelvis and balance the trunk over it. For almost all children this requires special guidance and training. Only a few, less than 5 per cent, develop good posture spontaneously.

[ED. NOTE.—Opinions differ on the subject of posture. Some writers state the belief that normal, healthy children usually develop normal posture without any postural training if their parents have normal posture. If less than 5 per cent of children develop good posture spontaneously, it is interesting to think what the posture of the world population must be, since a relatively small percentage of the population has the opportunity for special guidance and training.]

Howorth,<sup>1037</sup> in an extremely interesting and complete study of posture, presents his ideas on what he calls dynamic posture. He states:

Posture has long been thought of in terms of standing and sitting, and correct posture as the erect position assumed as one is under inspection, but posture should really be considered as the sum total of the positions and movements of the body throughout the day and throughout life. It should include not only the fundamental static positions in lying, sitting and standing and the variations of these positions but also the dynamic postures of the body in motion or in action, for it is here that posture becomes most important and most effective.

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1036. Kuhns, J. G.: Normal Posture in Early Childhood, *Pub. Health Nursing* **38**:406-410 (Aug.) 1946.

1037. Howorth, B.: Dynamic Posture, *J. A. M. A.* **131**:1398-1404 (Aug. 24) 1946.

The author describes the development of posture, reviewing the baby's posture as well as that of the child and the adult. The many variations of lying posture and the effect of various types of support and positions, including the hammock and various types of bedsprings and mattresses, are discussed, as are the sitting posture and the effect of various seats and supports.

The author considers the standing position as "a basic position from which constant changes are made rather than as a position continuously held." The characteristics of ideal posture at rest and for the dynamic position of expected forward movement are presented. Individual types of posture, poor posture and its causes and effects, and posture correction are discussed.

Dynamic posture is posture in motion or in action or in preparation for action. Good dynamic posture implies the use of the body or its parts in its simplest and most effective way, using muscle contraction and relaxation, balance, coordination, rhythm and timing as well as gravity, inertia and momentum to optimum advantage.

Movement is the basis of dynamic posture. Good dynamic posture is common to such animals as the cat and the horse and often to children and primitive man but is uncommon in adult civilized man.

[ED. NOTE.—This interesting approach to the problem of posture should be read by any one interested in the study of posture.]

#### PARAPLEGIA

Poer<sup>1038</sup> discusses the newer concepts in the treatment of patients paralyzed owing to injuries of the spinal cord and outlines a plan of treatment, giving a statistical analysis of the cases studied. He points out that whereas approximately 2,500 soldiers and sailors received such injuries in World War II, the final mortality rate may show a large decrease, from an all-time high for the Balkan Wars of 95 per cent (the average for other wars was 50 to 60 per cent) to approximately 20 per cent in the last war. Lowering of the battlefield mortality produced an increase in the number of patients to be cared for. The author discusses ways and means by which these patients can be restored to some type of ambulation.

In his statistical analysis of 77 cases in which the patients were treated within a fifteen month period, there were 15 cases of cervical involvement; 18, of involvement of the cauda equina in the lumbar area, and 5, of such involvement in the sacral area. The remaining 39 patients were injured in the region of the dorsal spine. Twenty-nine of the patients had complete transection of the cord.

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1038. Poer, D. H.: Newer Concepts in the Treatment of the Paralyzed Patients Due to War-Time Injuries of the Spinal Cord, *Ann. Surg.* **123**:510-515 (April) 1946.

Seventy-four per cent had serious emaciation, with an average loss of weight of 42.5 pounds (19.33 Kg.) per person. Forty-four patients had undergone primary laminectomy.

[ED. NOTE.—This is an interesting and extensive study of one of the most difficult problems in orthopedics—the paraplegic patient. It is interesting to note the number of laminectomies which were done. Though it is stated that the orthopedist treats the fractures and supervises the mechanical means of walking, nothing is said about spinal fusion in this series.]

Botterell and his associates<sup>1039</sup> report a study of paraplegic patients. The authors describe and illustrate long leg braces of chrome molybdenum, especially suitable for paraplegic patients, and custom-made, modified hockey cut-type boots which are light in weight and particularly flexible; the boots are recommended for prevention of pressure sores on the feet. A simple "bed exerciser" is also described. Paraplegic patients should be evacuated as early as possible to a center fully equipped and specially staffed to deal with all aspects of treatment and retraining. The authors emphasize the importance of enthusiastic cooperation of the patient and of all those attending him, pointing out that 'almost any patient with an injury to the spinal cord can be salvaged to occupy a useful place in society.

[ED. NOTE.—This, also, is an excellent study of the problem of the paraplegic patient. The authors discuss the treatment of the paraplegic casualty with a stable spinal column but do not go into the problem of the unstable spine and the indications for spinal fusion.]

Covalt<sup>1040</sup> discusses the rehabilitation, as planned by the Veterans Administration, of the patient with severe injury to the spinal cord. The author emphasizes five phases of treatment: neurologic, urologic, surgical, psychiatric and physical. He states that patients thus affected in the first World War usually died in a period of a month to a year and a half, and that only 1 such patient survived at the time of the report. With new drugs and improved surgical management, a modern medical rehabilitation program makes it possible for paraplegic patients to live as long as so-called normal people. At present there are 2,000 patients in this country with severe injuries to the spinal cord; the Veterans Administration has approximately 1,000 in its care. Paraplegic patients will be concentrated in five or six special centers of

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1039. Botterell, E. H.; Jousse, A. T.; Aberhart, C., and Cluff, J. W.: Paraplegia Following War, *Cincinnati J. Med.* **27**:595-623 (Sept.) 1946.

1040. Covalt, D. A.: The Rehabilitation of the Veteran with Severe Spinal Cord Injury, *Occup. Therapy* **25**:187-190 (Oct.) 1946.

the Veterans Administration. Special teams composed of a neurosurgeon, a physical therapist, physical therapy technicians, occupational therapists, supervisors of corrective physical rehabilitation, nurses and others will treat these patients.

The program as developed in the Veterans Administration includes specific and detailed training for the paraplegic so he may accomplish the 72 activities necessary for the physical demands of daily life. They range from (1) moving from place to place in bed, to (72) driving a car. There are 37 activities for non-walkers; 17 for walkers; 12 having to do with getting up and down; 4 for endurance and speed so as to keep up with the demands of daily life; and 2 for traveling by car or other suitable vehicle.

[ED. NOTE.—The author discusses the program in some detail, stressing the importance of medical, social and vocational treatment, and emphasizes occupational therapy and rehabilitation.]

#### SCOLIOSIS

Mol and van der Zijl<sup>1041</sup> discuss the influence of the abdominal muscles in the production of scoliosis. Lowman's operation of fascial transplantation for reenforcement of the weak or paralyzed abdominal muscles and the modifications of Mayer and of Dickson are discussed, and the authors present a modification of their own. They state that a patient with scoliosis not preceded with poliomyelitis merits examination of the abdominal muscles as well as one with a history of poliomyelitis, and that "after a minute examination one will find that many idiopathic scolioses are caused by a paralysis of the abdominal muscles." One case with operation according to Lowman's method and 3 cases in which treatment was by the authors' modification of Lowman's procedure are reported. They state the belief that their method has three advantages:

First, the "natural" insertion of the muscular sheath of fascia lata at the iliac crest;

Second, the greater solidity of the transplanted material containing as well contractile elements . . . even if the tensor fasciae latae degenerates;

Third, the reenforcement of a part larger than the weakened part.

[ED. NOTE.—Further evidence is necessary to support the authors' claim that in many cases idiopathic scoliosis is caused by paralysis of the abdominal muscles. The authors imply, as many others have, that the indicated treatment of scoliosis due to paralysis of the abdominal muscles following poliomyelitis (or even the treatment of idiopathic scoliosis) is a modification of the Lowman fascial transplantation,

1041. Mol, W., and van der Zijl, M. O.: Scoliosis Due to Paralysis of Abdominal Muscles, *Rev. d'orthop.* 32:151-159 (May-Aug.) 1946.

and many inexperienced orthopedic surgeons may be misled. Whereas fascial transplantation may aid weakened abdominal musculature following poliomyelitis in selected cases, it seems obvious that one cannot hold up a severely telescoping, unstable, segmented vertebral column, in any severe case of scoliosis following poliomyelitis, with fascial abdominal transplants. Spinal fusion is necessary in most severe cases if stabilization or prevention of further progress of the curve is to be expected. In many cases in which abdominal transplants seem indicated, it is found that the procedure is not necessary after adequate spinal infusion.]

Marique<sup>1042</sup> describes the use of a semibent plaster jacket in the treatment of scoliosis. He uses it especially in cases of a single curve, which he states constitute about 40 per cent of the total. He states the belief that his type of jacket is original, as he found no reference to the treatment in the literature.

[ED. NOTE.—The method has been used in this country for some years by a number of different orthopedic surgeons, although there is a variation in the way the jacket is applied. No one has as yet reported any extensive series of cases in which roentgenograms were made to prove the efficacy of this treatment. In my experience, a relatively small percentage of instances of idiopathic scoliosis are of the single curve type. Most patients with idiopathic scoliosis show more than one structural curve, and it is obvious that the application of a semibent jacket might be advantageous for one curve and not so good for the opposite one.]

## XXI. RESEARCH

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THE LITERATURE on orthopedic research and related subjects for 1946 shows a preponderance of articles on changes in the bone associated with hormones. However, there are no outstanding articles among this group. Seventy-one articles were abstracted for this review, and thirty-one have been selected as references. They are divided into the following subjects: (1) changes in the bone, associated with hor-

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1042. Marique, P.: Contribution au traitement de la scoliose, *Rev. d'orthop.* 33:61-64 (Jan.-March) 1947.

mones and other substances; (2) biochemical studies; (3) anatomic and physiologic studies; (4) studies of muscle; (5) studies of cartilage, fascia and joint; (6) fluorine studies, and (7) miscellaneous research.

CHANGES IN THE BONE, ASSOCIATED WITH HORMONES  
AND OTHER SUBSTANCES

M. and R. Silberberg<sup>1043</sup> state:

In immature male mice, testosterone propionate accelerated the ageing of the epiphyseal cartilage by inhibiting proliferation and by increasing regressive changes. These effects were less marked in males than in immature females. Removal of the testicles caused a delay in the development of the cartilage, followed by a reduction in the rate of proliferation. . . . Administration of small doses of testosterone propionate to castrate mice restored both development and growth of the epiphyseal cartilage. The resumption of growth is incidental to the restitution of the development of the cartilage and is not due to a direct growth-stimulating effect of the hormone.

It has been shown that both estrogenic and thyrotropic hormones accelerate skeletal aging in growing animals, although their effect is exerted on different phases of the skeletal time curve. Thyroxin has little effect on growth but hastens the resorption of cartilage and bone, leading to epiphysial and diaphysial union. Estrogen, however, suppresses growth and inhibits the resorptive processes. In the reported experiment, M. and R. Silberberg<sup>1044</sup> dealt with the combined action of the two hormones in young mice. Under combined therapy, the age changes in growth zones at any given stage were considerably advanced over those in untreated animals. After two months' observation, it was noted:

. . . the addition of thyroxin did not materially affect the decrease in the proliferation of the cartilage caused by estrogen; . . . On the other hand, the metaphyseal connective tissue was less hyalinized, and the bone present was less abundant and more loosely knit than after injections of estrogen only.

After 6 months of observation . . . resorption of the epiphyseal cartilage resembled closely the same processes seen after administration of thyroxin alone . . . [although less advanced]. . . . Resorption of bone in the shaft and metaphysis was more conspicuous after administration of both hormones than after that of estrogen alone.

It is therefore clear that the two hormones tend to compete with each other "in enforcing their characteristic changes on the skeletal time curve."

1043. Silberberg, M., and Silberberg, R.: Further Investigations of Effect of Male Sex Hormone on Endochondral Ossification, *Anat. Rec.* **95**:97-117 (June) 1946.

1044. Silberberg, M., and Silberberg, R.: Skeletal Changes Caused by Combined Administration of Thyroxin and Estrogen, *Am. J. Path.* **22**:1033-1045 (Sept.) 1946.



Benoit, Messerschmitt and Grangaud<sup>1045</sup> state that a daily injection of 1 mg. of estradiol benzoate in immature drakes causes abundant formation of bone in the marrow cavities of various parts of the skeleton, especially in the femur and tibia. The marrow reduces in volume and becomes less fatty and more hematopoietic. In proportion to body weight, the injection of estradiol benzoate causes a considerable increase in weight of the femurs and tibias. The blood calcium and phosphorus are increased for a few days and then slowly return to normal, even though injections are continued.

Sammartino and Terzano<sup>1046</sup> found that the daily injection of 1 cc. of estrogen (estradiol benzoate) into the leg muscle of 3 month old leghorn chickens for twenty-two days (a total of 220,000 international biologic units) caused an increase in the blood calcium and an increase in the bony trabeculae in the medullary cavity of the long bones (epiphysis and internal surface of the diaphysis in femur and tibia), with incomplete and imperfect ossification and defective absorption of cartilage.

[ED. NOTE.—The accumulation of experimental evidence on the formation of bone in animals, especially in the medullary cavity after the administration of estrogen, may be of great importance in explaining some of the unknown factors in ossification. Such an explanation might lead to important data to be used in the treatment of fragile bones, cystic disease of bone, osteomalacia or osteosclerosis.]

After the administration of pituitary growth hormone to hypophysectomized rats, Becks and his co-workers<sup>1047</sup> noted that osteogenic processes in the epiphyseal cartilage of the tibia were reawakened, even after postoperative intervals of a year or more:

Some response was obtained within 5 days, but daily doses of 200 to 400 mg., given for 25 to 30 days, were necessary for reestablishment of vigorous osteogenesis comparable to that seen in the normal, young, growing rat.

Thyroxin had a synergic effect on this response to growth hormone, provided only that the dose was low enough for it to be tolerated by these animals. Thyroxin alone stimulated some proliferation and enlargement of cartilage cells . . . but little osteogenesis.

Contrary to the results seen in the epiphyseal cartilage of the tibia, thyroxin was found to antagonize the effect of growth hormone on the cartilage covering the

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1045. Benoit, J.; Messerschmitt, J., and Grangaud, R.: Osteogenetic and Hypercalcemic Action of Estradiol Benzoate in Male Domestic Duck: Chemical Study, *Compt. rend. Soc. de biol.* **135**:1593-1596, 1941.

1046. Sammartino, R., and Terzano, G.: Bone Changes in Chickens Receiving Estrogens, *Prensa. méd. argent.* **33**:362-366 (Feb. 15) 1946.

1047. Becks, H., and Others: Response to Pituitary Growth Hormone and Thyroxin of Tibias of Hypophysectomized Rats After Long Postoperative Intervals, *Anat. Rec.* **94**:631-655 (April) 1946.

head of the tibia. This antagonism had previously been observed in the condyle of the mandible in the same animals.

[ED. NOTE.—The study of hormones as related to orthopedics is still in its infancy, and no important clinical application is evident at present. The use of thyroxin, estrogens or androgens to promote early epiphysial union may be feasible in the future. Apparently contradictory results reported by various investigators may be explained on the basis of difference in dosage. Small and large doses of the same drug in some instances produce opposite effects.]

Votansky, in 1930, succeeded in producing typical signs and symptoms of osteitis fibrosa cystica in dogs by means of injection of parathyroid extract. The dogs were fed a well rounded diet, including occasional administration of calcium salt. However, Burns and Henderson<sup>1048</sup> were unable to duplicate these findings under similar conditions, although the dogs were given a calcium salt regularly. The authors state the opinion that calcium intake is the most important single factor in the experimental production of hyperparathyroidism. In their experiments, administration of parathyroid extract in association with a low calcium intake resulted in a decrease in serum calcium nearly to the level for tetany. With higher calcium intake, the decrease did not occur. In neither instance was there any measurable chemical effect on bone growth or on decalcification. Even with a low level of serum calcium, the calcium content of bone was not appreciably disturbed. In puppies, the amount of calcium laid down in bones and the level of serum calcium varied directly with the calcium intake. It is the authors' opinion that the parathyroid gland influences both the building up and the breaking down of bone, as suggested by other investigators, but the final equilibrium between bone calcium and blood calcium is determined by activity of bone cells and by calcium intake.

In experiments conducted on hypophysectomized rats, Reiss, Fernandes and Golla<sup>1049</sup> showed that large doses of testosterone propionate definitely inhibited the action of the growth hormone. In addition, increase of body weight was less when the androgen was given in conjunction with the growth hormone. Testosterone propionate itself, given in doses of 4 mg. daily, did not affect growth or influence the decrease in weight usually noted after hypophysectomy. A dose of 0.1 mg. of estrone produced similar results, and 2 mg. of desoxycorticosterone acetate, effects somewhat similar. The results of the investigations showed that large doses of testosterone propionate had an inhibitory

1048. Burns, C. M., and Henderson, N.: Mineral Constituents of Bone: Effect of Prolonged Parathormone Injections on Composition of Bones of Puppies with Varying Calcium Intakes, *Biochem. J.* **40**:501-507, 1946.

1049. Reiss, M.; Fernandes, J. E., and Golla, Y. M. L.: Peripheral Inhibitory Influence of Large Doses of Testosterone on Epiphysial Cartilaginous Growth, *Endocrinology* **38**:65-70 (Feb.) 1946.

effect on the cartilaginous activity of the growth hormone; this might be explained on the basis of increased circulation and increased calcification. Other workers have demonstrated an opposing or synergistic effect between administration of growth hormones and small daily doses (0.05 to 1.0 mg.) of testosterone.

In modern traumatology, insufficient attention has been given to new methods for stimulating regenerative osteoblastic reaction in the treatment of fractures. Positive results in such experiments have hitherto been lacking. Clinical observations indicate that even when all other conditions are the same, such as the type of fracture, the method of conservative treatment and the age of the patients, the time of consolidation of the fracture and the function of the growing callus often differ considerably. Thus a difference in the reactivity of the connective tissue cells involved in callus formation is clearly indicated. Bogomolets,<sup>1050</sup> in his work, has sought a method to stimulate regenerating osteoblastic action. He analyzes the effect of the antireticular cytotoxic serum on the consolidation of bones after fracture in experimental and clinical cases. It was suspected that the stimulating effect of antireticular cytotoxic serum, previously observed on some of the cellular elements of the connective tissue system, might also occur in the osteoblastic elements, and the suspicion was confirmed. In small stimulating doses, serum exerts an intensive and specific effect on acceleration of regeneration of osseous tissue. By use of the serum, the author has been able to obtain bone union in fractures considered hopeless. The effects of the serum on the cellular elements of the connective tissue system, such as the osteoblasts, vary with the dose administered. Large doses have an inhibiting effect on the cellular elements at the site of the fracture. Animals receiving large doses of the serum showed other pathologic conditions, such as low resistance to infection and, in some instances, progressive cachexia. Small doses also yielded good results in cases of retarded callus formation after fracture in both young and old persons. In older patients, there was pronounced improvement in general condition.

The histogenesis of the callus under stimulation with antireticular cytotoxic serum shows that there is active formation of osteoblasts, with accelerated transformation into osteocytes, which plays an important part in the acceleration of bone formation. For an average therapeutic dose, 0.07 cc. of undiluted serum, with a titer of 100 to 120, is recommended. The dose is injected subcutaneously at intervals of two to three days. The test with trypan blue is recommended for judging the stimulating effect of the serum.

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1050. Bogomolets, O. A.: Effect of Antireticular Cytotoxic Serum on Histogenesis of Bone Callus, *Med. zhur.* **12**:283-291, 1944.

The use of the serum for the treatment of fractures requires careful observation of the process of repair by the attending physician, since the union may take place so rapidly that an accurate reposition of the fragments may not have been obtained.

In an attempt to corroborate the results of Bogomolets' work concerning the effect of antireticular cytotoxic serum on the healing of fractures, Straus and his co-workers<sup>1051</sup> carried out an experiment: Antireticular cytotoxic serum was prepared by injection of rabbit spleens and bone marrow antigen into goats. The radius and ulna of 156 rabbits were fractured experimentally with a Grattan osteoclast. The fractures were immediately reduced and immobilized. Three days after operation, the rabbits were arbitrarily divided into four groups: Group A received small stimulating doses of antireticular cytotoxic serum; group B received large doses of the same serum, and groups C and D were composed of control animals, which received small and large doses of goat serum.

The results were graded according to roentgenographic evidence of callus on the seventh, tenth and fourteenth days; gross postmortem evidence of bone and callus formation; microscopic examination of bone at the fracture site, and breaking point of bone at the fracture site, determined by subjecting the bone to a mechanical strain.

The animals in group A, which received small doses of antireticular cytotoxic serum, showed roentgenographic evidence of callus earlier than those in any other group; the callus was also greater in amount. Post-mortem examination revealed similar changes. Microscopic examination showed a greater degree of new bone formation. The breaking point of the bones of these animals was the highest in all groups, the average force required being 7,000 Gm. Animals in group B, which received large doses of antireticular cytotoxic serum, showed least evidence of new bone formation on roentgenographic and microscopic examination, and the lowest breaking point (680 Gm.). Ratings of control groups C and D were intermediate between those of groups A and B, with an average breaking point of 3,365 Gm.

The authors state the opinion that the results did corroborate the work of Bogomolets.

[ED. NOTE.—The results of the work of Bogomolets and their corroboration by Straus and his co-workers may be of definite clinical significance in the treatment of slowly healing and ununited fractures. The procedure needs a great deal more study before it can be used routinely if the statement of Bogomolets, that the process of repair may be so greatly accelerated that an accurate reposition of fragments may not have been obtained before union is complete, is correct.]

1051. Straus, R., and Others: Studies on Antireticular Cytotoxic Serum: III. Effect of ACS on Healing of Experimentally Produced Fractures in Rabbits. *J. Immunol.* **54**:163-177 (Oct.) 1946.

## BIOCHEMICAL STUDIES

Tarantino<sup>1052</sup> showed that immobilization of the hindlimbs of rabbits in plaster casts produces a significant increase in blood calcium, and a significant reduction in phosphorus, potassium and magnesium. These changes subside in fifteen to thirty days after removal of the cast, to reach normal levels. The author attributes the changes to functional inactivity.

In a preliminary discussion of their investigations, Baker, Butterworth and Langley<sup>1053</sup> emphasize the constancy of calcium in bone per unit weight. In pathologic conditions, such as rickets or osteomalacia, produced either by a vitamin D deficiency or by a lack of calcium phosphate, there is interference with the calcifying process so that osteoid tissue fails to calcify normally. In no other known disease, however, is there histologic evidence of calcium deficiency in bone substance. The term "decalcification," rather loosely used to describe such conditions as osteoporosis, describes a process which is in reality and histologically a deossification. Protein matrix and calcium are removed together. The bone which remains is normally calcified. In fibrosis of bone, as fibrous dysplasia, bone is actually replaced by fibrous tissue.

In the investigations, bone was taken from the cortex of the adult femur, the cancellous portion of the adult femur, the adult rib, the infant rib and, in 6 cadavers, from sequestrums. The bone was thoroughly cleaned, defatted and dried, after which estimates of calcium and nitrogen were made. No significant differences were found in the content of calcium and nitrogen in the cortical or cancellous bone of the femur or in the sequestrums. The infant rib contained more nitrogen and less calcium than the adult rib, a condition which might have been expected. The authors could not explain the significantly high nitrogen content in the adult rib as compared with that in the adult femur. The ratio of calcium salt to protein averaged 2.5 for sequestrums, 2.4 for cortical bone, 2.3 for cancellous bone of the femur, 2.1 for adult rib and 1.9 for infant rib.

[ED. NOTE.—The study of the nitrogen content and the other organic portions of bone represented by the protein matrix is an almost untouched field of research. It is to be hoped that in the future more research workers may direct their attention to this portion of the bone, which constitutes approximately one third of the bone by weight and two thirds by volume.]

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1052. Tarantino, A. M.: Contributions to the Study of Various Chemicals of Muscle During Mechanical Immobilization and the Subsequent Functional Reactivation: Variations of Calcium, Phosphorus, Potassium and Magnesium, *Med. sper., Arch. ital.* **10**:257-269 (Aug.) 1942.

1053. Baker, S. L.; Butterworth, E. C., and Langley, F. A.: Calcium and Nitrogen Content of Human Bone Tissue Cleaned by Micro-Dissection, *Biochem. J.* **40**: 391-396, 1946.

Feeding experiments were carried out by Nordfeldt<sup>1054</sup> on pigs, the diet of which consisted of grain, such as barley, oats and corn, and 2.5 Kg. of skimmed milk daily. In some cases calcium, phosphorus or activated 7-dehydrocholesterol (vitamin D<sub>3</sub>) was added to the diet. The experiments took place over a three months' period, during which time the weight of the animals rose from 35 Kg. to 100 Kg. When calcium or phosphorus or both were added to the diet, a decrease in the fat content of the femur was noted. Activated 7-dehydrocholesterol, however, appeared to increase the fat content of the same bone. When calcium or phosphorus was given simultaneously with the activated 7-dehydrocholesterol, the increase in fat content was less. It thus appears that calcium or phosphorus, on the one hand, and activated 7-dehydrocholesterol, on the other hand, counteract each other in influencing the fat content of the skeleton.

Holmes and his co-workers<sup>1055</sup> assayed twenty-four samples of goat's milk and found that the values were: calcium, 137 mg. per hundred grams; magnesium, 17 mg.; potassium, 170 mg.; phosphorus, 112 mg.; fat, 4.4 per cent, and protein, 3.4 per cent. Goat's milk contains two to three times as much protein and over three times as much ash as does human milk, but there is present only two-thirds the amount of lactose in human milk and essentially the same amount of fat, iron and copper. The studies show that goat's milk has a mineral content much higher than that reported for human milk, and somewhat higher than that reported for cow's milk. However, the extent to which infants can utilize the additional minerals supplied by goat's milk is as yet an unanswered question.

[ED. NOTE.—The administration of raw goat's milk might be worth while in cases of evident deficient mineral content of bone, and it might be helpful in cases of ununited fracture in which the blood calcium is low.]

Brandenberger and Schinz<sup>1056</sup> performed a systematic investigation of calcification in the human body and studied the relationship between inorganic bone substance and various diseases of bone. The results were based primarily on roentgenologic study of the finer structure of calcification. The first part of the monograph is devoted to a review of the fine atomic structure of the involved combinations of calcium and is

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1054. Nordfeldt, S.: Influence of Phosphorus, Calcium and Vitamin D<sub>3</sub> upon Fat Content of Skeleton in Growing Pigs, *J. Nutrition* **31**:565-572 (May) 1946.

1055. Holmes, A. D.; Kuzmeski, J. W.; Lindquist, H. G., and Rodman, H. B.: Goat's Milk as a Source of Bone-Building Minerals for Infant Feeding, *Am. J. Dis. Child.* **71**:647-653 (June) 1946.

1056. Brandenberger, E., and Schinz, H. R.: Nature of Calcifications in Man and Animals and Behavior of Inorganic Bone Substance in the Case of Chief Human Bone Diseases, *Helvet. med. acta (supp. 16)* **12**:1-63, 1945.

followed with a review of roentgenologic findings in 80 human skeletons, normal and diseased, and in thirty different animal species.

The authors review the present status of roentgenologic study of the inorganic components of normal bones and teeth and finally present a summary of the nature and condition of the crystals encountered. They were struck by the fact that all the varied types of calcification in normal and diseased bone showed uniform crystals. In attempting to determine the chief types of crystals in different calcification processes, they found that in all pictures there was one and the same type, possibly due to the fact that the organism, in precipitating calcium salts in most varied conditions and locations, tends to one type of medium, with a resulting uniform type of crystal. In man and vertebrate animals, the apatite form of crystal hydroxyl (apatite) predominates. Apatite structure is absent from all nonvertebrates in which the predominant form of crystal is calcite. In vertebrates, calcite crystal is found only in pancreatic stones and in the calcium portion of gallstones. Physiologically, calcite is found in man only in otoliths. No exception to the rule was observed in the various bone diseases, such as rickets, renal rickets or various types of osteomalacia. Apatite crystals were found in the teeth of vertebrates.

Roche and Mourgue<sup>1057</sup> showed in experiments that the excess of phosphorus in embryologic bone specimens before the appearance of points of calcification is composed almost exclusively of the radicals  $\text{PO}_4$ , which are easily ionizable and doubtless fixed to the protein matrix. The bone salts in the same organs contain a mixture of bicalcic phosphates and tricalcic phosphates, whereas in well calcified embryonic specimens one finds only tricalcic phosphorus. In skeletal tissue taken from sheep embryos before the beginning of calcification, orthophosphoric acid ( $\text{H}_3\text{PO}_4$ ) is present, in feebly ionized form and probably bound to the protein matrix. The first bone salt is a mixture of dibasic calcium phosphate ( $\text{CaHPO}_4$ ) and tribasic calcium phosphate ( $\text{Ca}_3 [\text{PO}_4]_2$ ); later only tribasic calcium phosphate is found.

Ankyloses of joints should not be considered merely as local lesions. In reality, ankylosis reflects a profound upset in the life of the bone. Cretin and his co-workers<sup>1058</sup> visualize circulation across the epiphysal line, whereby nourishment and waste products are continually interchanged between epiphysis and diaphysis. The authors state the belief that when the filter becomes obstructed, waste products, such as fat particles and oil, accumulate and interfere with the function of the joint.

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1057. Roche, J., and Mourgue, M.: First Stages of Ossification and Formation of Bone Salt, *Compt. rend. Soc. de biol.* **137**:451-452, 1943.

1058. Cretin and Others: Contributions to the Histochemical and Therapeutic Study of Certain Types of Ankyloses, *Bull. Acad. de méd., Paris* **130**:257-258 (March 26-April 9) 1946.

Therefore, by surgical intervention, such as drilling, a communication may be reestablished between the epiphysis and the marrow cavity of the diaphysis. Several cases are reported in which good results were obtained by this method of treatment, in ankylosis of the knee joint following fracture and in ankylosis of the hip, associated with rheumatoid arthritis; relief from pain was obtained by this operative procedure, which is not discussed in any detail. Apparently, direct communication is established between joint and marrow cavities.

[ED. NOTE.—It is difficult to imagine how the establishment of a communication between a joint and a marrow cavity or between an epiphysis and a diaphysis can affect ankylosis following fracture or associated with arthritis or, especially, affect pain, if present. The problem needs further study.]

#### ANATOMIC AND PHYSIOLOGIC STUDIES

Davies<sup>1059</sup> has made a thorough study of the anatomy and physiology of diarthrodial joints, with the following conclusions: The tissue composing diarthrodial joints arises from mesodermal elements; the joint cavity develops by liquefaction of mesenchymal tissue. The joint capsule, the periosteum and the perichondrium are composed of tough, inelastic, white fibrous tissue, which has good resistance to infection but poor powers of repair. The synovial membrane is soft, elastic and movable, with good nerve and blood supply and good phagocytic power.

Articular cartilage is smooth, elastic, devoid of sensation and avascular. It has no demonstrable blood or nerve supply. Between the articular cartilage and bone there is a zone of calcified cartilage. The cartilage cells toward the periphery are flat and small and continually removed by constant wear; thus, the cell content of cartilage decreases with age, and the amount of matrix increases proportionately. The metabolic requirements of cartilage are low. Lesions of the articular cartilage over weight-bearing surfaces have little tendency to repair. At the articular margins, repair may be aided by synovial ingrowth. Apposition of articular surfaces is essential to normal function of articular cartilage. Loss of apposition, as in congenital dislocation, leads to degeneration of the cartilage and formation of fibrous tissue.

Synovial membrane is defined as modified connective tissue. It covers all joints except the cartilage in weight-bearing areas. The underlying connective tissue is important in its quality and quantity and determines the mobility of the synovial membrane. The membrane is supplied with elastic tissue fibers, which are not present in the villi.

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1059. Davies, D. V.: *Anatomy and Physiology of Diarthrodial Joints*, *Ann. Rheumat. Dis.* 5:29-35 (Dec.) 1945.



After synovectomy, the lining is reformed by metaplasia of connective tissue, but the new lining probably does not preserve the special characteristics of synovia and the fluid is probably considerably modified.

The blood supply is quite rich, is situated superficially and arises from anastomotic branches of the main arteries nearby. Communications exist between the blood vessels and those of the adjacent epiphysis. Simple bruising over a joint is frequently associated with hemorrhage into the synovial cavity. A single lymphatic plexus lies in the synovial membrane, but lymph vessels are not so numerous as the blood vessels. No direct communication exists between the cavity of the joint and the lumen of the lymphatics.

According to Hilton, the same trunks of nerves whose branches supply the group of muscles moving a joint also supply nerves to the interior of the joint, and to the skin over the insertion of the muscles. The nerve supply of joints accompanies the arteries.

Solutions of particles of small molecular dimensions pass rapidly in either direction across the synovial barrier, mainly through a blood capillary bed. The lymphatic system plays a minor role in the process. The synovial fluid differs in physiologic, chemical and cytologic character from joint to joint. Albumin and globulin occur in the fluid in a 4:1 ratio, showing a much lower concentration than that in the serum. There is no fibrinogen in the joint fluid; consequently, it does not clot. Mucin can be precipitated, however. It is thought to be a secretion of synovial cells. Urea and amino acids appear in essentially the same proportion as in the blood. There is less glucose, however, and the level falls with an increased cell count in the synovial fluid. The levels for chloride and carbon dioxide are high, that for inorganic phosphate is approximately the same and those for sodium, potassium and magnesium are lower in comparison with blood levels. The level for calcium is high as compared with the blood; in conditions causing increased capillary permeability, the calcium content of the synovial fluid is further increased.

Red cells do not occur normally in the joint fluid. Monocytes and plasmacytes predominate, though lymphocytes are present in small numbers. The average cell count is 63 per cubic centimeter; degenerative changes cause an increase in the cell count.

[ED. NOTE.—The article, although contributing no essentially new information, does contain an excellent summary of the anatomy and physiology of diarthrodial joints.]

In a report of a study of the blood supply and lymphatic drainage of tendons, Edwards<sup>1060</sup> states:

Almost the whole of the tendon is made up of collagen fibrils closely packed together, and apparently undergoing little or no metabolic activity. The living

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1060. Edwards, D. A. W.: Blood Supply and Lymphatic Drainage of Tendons, *J. Anat.* 80:147-152 (July) 1946.

part of the tendon consists of the tendon cells lying between the bundles of collagen fibrils they have produced, and the interfascicular connective tissue. It is these living tendon cells which require a blood supply.

[Each] tendon and its synovial sheath have one artery in the center, on each side thereof a vein, and the lymphatic vessels disposed as four main channels one on each side of each vein.

There are no valves . . . in the veins or lymphatics on the visceral synovial membrane, though they occur in the mesotendons.

There is a rich anastomosis in the lymphatic and venous systems. It is known that tendon is resistant to infection, can be transplanted and heals well as a result of excellent longitudinal anastomosis of blood vessels and frequent feeding by the synovia. Suture of a tendon within a synovial sheath is usually followed with adhesions. The author suggests that inversion of the edges of the sheath, as is done with peritoneum, may lower the incidence of adhesions after suturing.

[ED. NOTE.—This is a worth while and practical anatomic study.]

In a series of three articles, Mac Conaill<sup>1061</sup> presents a well written, highly complicated mathematical discussion of the mechanics of joint motions. Geometric factors are considered which determine the effect on a bone of successive movements at a joint. Such terms as cardinal movements, circumductions, conjunct and adjunct rotation and diadochal movements are defined and used to explain joint motion. Illustrations are given in experiments on the shoulder joint. In the two latter articles, an even more detailed study is made of the mechanics of saddle joints and hinge joints. The results of the experiments are presented, with numerous diagrams and mathematical formulas.

The variations of the tendo achillis were studied in a group of 100 autopsies by Cummins and his co-workers.<sup>1062</sup> Observations of the plantaris muscle were made in 50 specimens. Rotation of the fibers of the gastrocnemius muscle to the lateral side of the tendon, as first described by White, was confirmed in every case, although the rotation was of varying degree. Because of this peculiarity of the tendon a method of subcutaneously cutting the tendon is suggested which permits all the tendon fibers originating from both the gastrocnemius and soleus muscles to be cut without complete division of the tendon. A proximal section of the posterior two thirds of the tendon (the gastrocnemius portion) is

1061. Mac Conaill, M. A.: *Studies in Mechanics of Synovial Joint: Fundamental Principles and Diadochal Movement*, Irish J. M. Sc., June 1946, pp. 190-199; *Studies in Mechanics of Synovial Joints: Displacements on Articular Surfaces and Significance of Saddle Joints*, *ibid.*, July 1946, pp. 223-235; *Mechanics of Synovial Joints: Hinge Joints and Nature of Intra-Articular Displacements*, *ibid.*, Sept. 1946, pp. 620-626.

1062. Cummins, E. J., and Others: *Structure of Calcaneal Tendon (of Achilles) in Relation to Orthopaedic Surgery, with Additional Observations on Plantaris Muscle*, Surg., Gynec. & Obst. **83**:107-116 (July) 1946.

first made. A distal section is then made, in which the medial two thirds (the soleus portion) is divided. The plantaris tendon is also sectioned. In this way, all the fibers are severed either proximally or distally, except in those cases in which there is virtually no rotation of the tendon. In such cases, the few remaining lateral fibers of the soleus are easily torn.

A series of male mice were subjected by Lanier<sup>1063</sup> to daily, moderate, forced exercises from the age of 6 weeks for an average of twelve and a half months. A second series of mice, used as controls, were deprived of as much exercise as possible. The animals were killed at the end of the experiment:

The controls were found to have more minor lesions in the articular cartilage than the workers. There was no difference in the incidence of the more severe lesions or of ossification of the patellar ligament. It is concluded that exercise is not an important factor in occurrence of articular degeneration in mice, and that muscular activity does not affect the formation of a bony crest at the attachment of the patellar ligament.

[ED. NOTE.—Perhaps human cartilage, also, would be better preserved with more joint exercise than the average person takes; the joints might remain more normal to a later period in life.]

#### STUDIES OF MUSCLE

In a study on the effect of electrical stimulation on atrophy and recovery of the gastrocnemius, Kosman, Osborne and Ivy<sup>1064</sup> prepared rats by crushing the sciatic nerves bilaterally at the sciatic notch. One group of rats had muscular tension in each leg measured regularly by an isometric myograph. They were killed at fourteen, twenty-one, twenty-eight, thirty-five and forty-two days and the weight of the muscles in the legs determined. Another group had one leg stimulated with a current producing forty contractions per minute for five minutes, twice a day; they were similarly killed. Comparisons were made also of weight and tension between the stimulated and the unstimulated leg and between the legs of treated rats and those of the controls. Tension was more sensitive than weight as an index of muscular repair. Stimulated muscles were heavier and stronger during both denervation and recovery. The experiment does not prove conclusively that earlier functional recovery is caused by stimulation; however, it is assumed that the muscle returns earlier to normal use when atrophy is prevented. When stimulation is delayed until a muscle fiber is reinnervated, it is of no

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1063. Lanier, R. R.: Effects of Exercise on Knee Joints of Inbred Mice, *Anat. Rec.* **94**:311-321 (March) 1946.

1064. Kosman, A. J.; Osborne, S. L., and Ivy, A. C.: Effect of Electric Stimulation Upon Course of Atrophy and Recovery of Gastrocnemius of Rat, *Am. J. Physiol.* **145**:447-451 (Feb.) 1946.

value; nevertheless, stimulation should not be discontinued at the first sign of neurotization.

[ED. NOTE.—This evidence is certainly in favor of early daily electrical stimulation of muscles paralyzed due to injury to peripheral nerves; it confirms the results obtained by Hines, Melville and Wehrmacher (*Am. J. Physiol.* 144: 278-283 [July] 1945).]

#### STUDIES OF CARTILAGE, FASCIA AND JOINT

The object of a study by Jones<sup>1065</sup> and others was to determine the usefulness of curare in the differentiation of organic and functional factors in the limitation of passive motion at joints. Seventeen patients showing limitation of passive motion of joints were given curare intravenously in the form of purified chondrodendron tomentosum extract (intocostin®) after the usual subcutaneous doses of morphine and atropine. The intocostin® was injected into the antecubital veins in such amounts as to render the patient unable to lift his head from the table. In each instance, the procedure produced weakness of the hand grip and of the thigh muscles. Initial doses varied from 20 to 50 mg. Additional curare was injected at intervals of two to four minutes, to produce the desired effect. Eight patients showed increased range of motion while under the effect of curare, while 9 showed no significant change. In 5 of 7 cases of fracture in which patients showed increase in range of motion after administration of curare, the improvement was retained in full or in part, which suggests the possibility of using this drug as an adjunct to treatment in some cases. Curare can relieve pain by causing relaxation of muscle spasm.

[ED. NOTE.—These observations add to our already extensive knowledge of the use of curare. The drug will undoubtedly, at some time in the future, have an established place in the treatment of many orthopedic conditions.]

A series of 6 dogs were subjected by Hudack<sup>1066</sup> to an operation in which the head of the humerus was resected and replaced with a metallic head of a chrome-nickel steel alloy. One of the 6 dogs was allowed to live more than five years after operation. Weight bearing on the operated leg started at one month; at three months the animal had full and apparently normal activity, although there was approximately 10 per cent limitation of motion in the affected limb. In five years, there was 20 to 50 per cent limitation of rotation but no roentgenographic evidence of arthritis.

1065. Jones, C. W.; Le Compte, C. B., and Kabat, H.: Studies on Neuromuscular Dysfunction, VIII: Use of Curare to Differentiate Muscle Spasm from Organic Changes in Limitation of Passive Motion of Joints, *South. M. J.* **39**:799-804 (Oct.) 1946.

1066. Hudack, S. S.: Study in Articular Replacement, *Ann. Surg.* **124**:277-287 (Aug.) 1946.

At postmortem examination there were noted some thickening of the joint capsule and slight hypertrophy of the glenoid cartilage. The replacement element was firmly fixed in place and was not eroded or rusted; on removal, the underlying part of the humeral shaft was covered with a smooth, fibrous membrane, under which was smooth, homogeneous, noncancellous bone. In non-weight-bearing areas there was dense, stratified connective tissue, lying on flat bone trabeculae. In areas of weight bearing with stress due to compression the adaptive tissue was found to consist of fibrocartilage, whereas in the region of less stress, the fibrocartilage and fibrous elements combined. Foreign body reaction was absent. Further investigation into adaptive function is suggested.

[ED. NOTE.—This is a most important study of the use of foreign material in reconstructive bone surgery. It partially answers such questions as: What happens to the end of the bone, the surrounding fibrous tissue and the remaining cartilage in the joint?]

Prior to the study by Chandy,<sup>1067</sup> the work of a number of investigators (principally Nageotte) had led to the belief that dead tissue, such as a fascial graft, is incorporated into living tissue without foreign body reaction by a process of revivescence. It was thought impossible to distinguish the graft from the surrounding tissue after a certain lapse of time, during which fibroblastic activity and formation of new blood were constantly going on.

The author, in a series of experiments, transplanted alcohol-preserved ox fascia in human beings and examined the tissue microscopically at varying periods from one week to four years after operation. Though the graft became rapidly attached to the human tissue, it was gradually replaced, over a period of time, by ingrowth of capillaries and fibroblasts and by human connective tissue. The process, however, was still incomplete after four years. The fascial graft was found to provide a lattice or framework, on which normal human tissue might grow. The findings of the author are somewhat at variance with the theory of Nageotte, who conceived of the graft as uniting or healing with living tissue.

[ED. NOTE.—The study shows that transplanted fascia provides only a framework on which normal tissue grows, which is similar to the role of transplanted bone.]

#### FLUORINE STUDIES

A condition in rats characterized by protrusion and mottling of incisor teeth has been diagnosed by Pande,<sup>1068</sup> from histologic examination of teeth and bones, as fluorine intoxication. The condition

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1067. Chandy, J.: Fate of Preserved Heterogeneous Grafts of Fascia When Transplanted into Living Human Tissues, *Surg., Gynec. & Obst.* **83**:145-149 (Aug.) 1946.

1068. Pande, P. G.: Dental and Osseous Changes in Spontaneous Fluorosis in Rats, *Indian J. M. Research* **33**:121-128 (May) 1945.

occurred spontaneously in a colony of rats maintained on a diet which presumably contained a toxic dose of fluorine. The fluorine concentration in the bones of some of the rats was much higher than in those of animals kept on a low fluorine ration. Histologic changes in bones, such as osteoporosis, and in teeth in the spontaneous cases correspond closely in experimentally induced cases.

Fluorine is known to affect the tooth buds, but not adult teeth. The teeth of animals fed fluorine when young show mottled enamel when they erupt. Mostyn<sup>1069</sup> conducted experiments on pregnant dogs, which were fed on a diet containing large amounts of fluorine. Roentgenographic examination showed massive periosteal bone formation on the old cortex, especially in the long bones. In the case of puppies from a mother who has been on a fluorine diet, there were a blurred outline of the cortex of the bone and evidence of osteoporosis. The marrow cavity of the bones of the mother showed narrowing due to osteosclerosis. Cortical bone surfaces were rough, uneven and chalky, and extremely hard, though the bones of the offsprings were quite soft. Eruption of the permanent teeth was delayed. Experimental fluorosis could not be prevented or alleviated with an antirachitic diet.

#### MISCELLANEOUS RESEARCH

Zubiaurre<sup>1070</sup> demonstrated that the most significant roentgenologic features in alkaptonuric arthrosis are a productive, hypertrophic osteo-articular lesion, limited localization of the arthrosis in the hips, shoulders and spine, predominant involvement of the vertebral disk, showing calcification, and disappearance and changes in the vertebral bodies, showing deformation, decalcification or condensation and large production of osteophytes.

Experiments were performed by Lattes and Frantz<sup>1071</sup> on dogs to determine the effect of oxidized cellulose, fibrin foam and absorbable gelatin (gelfoam®) sponges on the healing of fractures. Oxidized cellulose in the vicinity of the fracture definitely interfered with normal bone repair. The mechanism of the interference was not definitely understood, but the presence of basophils in the tissue after introduction of oxidized cellulose suggested that a lowering of the local  $p_H$  might have been responsible by preventing the precipitation of inorganic calcium salt.

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1069. Mostyn, H. J.: Fluorides: Chronic Fluorine Intoxication; Effect on Bones and Teeth, *Vet. Med.* **41**:408-409 (Nov.) 1946.

1070. Zubiaurre, L.: Radiologic Aspects of Alkaptonuric Arthrosis, *Prensa méd. argent.* **33**:1383-1387 (July 5) 1946.

1071. Lattes, R., and Frantz, V. K.: Absorbable Gauze in Bone Surgery: Experimental Studies Suggesting Clinical Application in Reconstruction of Joints, *Ann. Surg.* **124**:28-39 (July) 1946.

In clean bone surgery when rapid formation of callus is desired, fibrin foam or gelfoam® sponges are to be preferred to oxidized cellulose. It is thought that the former substances interfere with bone formation to a lesser extent. The use of oxidized cellulose in arthroplasty or other procedures, in which bone repair is not desired, is suggested.

[ED. NOTE.—Oxidized cellulose should have a place in reconstructive bone surgery, when minimal new bone formation is desired. Fibrin foam or gelfoam® sponges should be useful in the control of bone bleeding, especially in surgery of the spine.]

## XXII. FRACTURE DEFORMITIES \*

Prepared by

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WAR AND civilian casualties have in the past few years afforded an unprecedented number of serious, complicated injuries and diseases of the myoneuroskeletal system. During the same period of time, many new and radically different methods and medicaments have been advanced in the treatment of these conditions.

Reports on the use of, and results obtained with, these new methods and materials have been numerous, widely distributed and not without variance. The collective experience and results obtained yet await critical evaluation. Many basic or fundamental principles are manifest when the reports of the various authors are analyzed.

### EARLY TREATMENT

In early treatment, says Renou,<sup>1072</sup> débridement with adequate excision of damaged soft tissue, minimal removal of comminuted bone, production of efficient drainage and complete immobilization of the affected parts are most essential. Tension in the closure of the soft tissues often means loss of life or of limbs.

Blood transfusions to combat shock and the use of penicillin combined with sulfonamide drugs permitted early secondary suture, or what might perhaps better be designated delayed primary suture, of wounds. The routine greatly lessened the number of severe infections and shortened the time required for healing, so that many men were returned to active duty who otherwise would have required long hospitalization.

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\* The first part of this review, by Leonard T. Peterson, M.D., and C. Glenn Barber, M.D., appeared in the ARCHIVES OF SURGERY for December 1948 (57: 855-870).

1072. Renou, C. A. M.: Early Treatment of Battle Casualties of Soft Tissues and Bone, Australian & New Zealand J. Surg. 15:193-205 (Jan.) 1946.

The author describes in detail the manner in which the several medications and procedures were introduced.

#### PENICILLIN THERAPY

Abbott and his co-workers<sup>1073</sup> report 8 cases in which free bone grafts were implanted in infected bone defects in conjunction with penicillin therapy. The authors state the opinion that it is probably more desirable, in most instances, to attempt to obtain healing with penicillin therapy preliminary to the grafting procedure. The report includes data on the site from which the donor graft was obtained, the method of fixation of the graft, the types of organisms present in the infected area, the dose of penicillin, the duration of penicillin therapy and a summary of each case. It is concluded that adequate dosage with penicillin is a useful adjunct in all cases in which bone grafting and other operations are done in areas in which there are bone defects infected with penicillin-susceptible organisms.

In an attempt to evaluate bone grafting operations performed without the use of penicillin and operations in which penicillin therapy had been used, Branch and Moldavsky<sup>1074</sup> present reports of 93 cases in which bone grafting operations were deemed advisable to facilitate union. Fifty operations were performed before penicillin was available for use, and 43 were performed when it was used. The 93 patients represented about 3 per cent of 3,000 patients with war fractures treated in the same United States Army general hospital. The cases in which operation was performed are presented in separate groupings, according to simple or compound fractures and treatment (with or without the use of penicillin). The cases in which penicillin therapy was commenced immediately after the operation and those in which it was commenced two days prior to the operation are listed separately. Postoperative infection developed in 8 cases. There were 4 postoperative infections (8 per cent) in the 50 cases in which no penicillin therapy was used; the end results in the group were: 48 cases, good; 1, fair, and 1, failure. In the 43 cases in which patients received penicillin, there were 4 instances of postoperative infection, or 9.3 per cent; the end results were: 42 cases, good, and 1, failure. The authors state the belief that infection was less disturbing and that healing of wounds was best in those cases in which penicillin therapy was begun two days preoperatively.

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1073. Abbott, L. C., and others: Use of Penicillin Therapy in Conjunction with Free Bone Grafting in Infected Areas, *Surg., Gynec. & Obst.* **83**:101-106 (July) 1946.

1074. Branch, H. E., and Moldavsky, L. F.: Penicillin and Bone Grafting Operations: Evaluation of Operations Performed Without Penicillin and Those Performed With Penicillin, *Mil. Surgeon* **99**:25-31 (July) 1946.



[ED. NOTE.—The material presented and the conclusions drawn in this report are worthy of detailed study and careful evaluation.]

Delayed osteosynthesis in conjunction with the administration of penicillin in 12 cases of irreducible open fracture is reported by Arnulf and others.<sup>1075</sup> Discussion is limited to but 10 cases, in which fifty or more days had elapsed after the patient received the war wound. Detailed reports of 6 cases are presented. In 5 of these, the fractures were due to projectiles; 1 was the result of a motor accident. The osteosynthesis was performed ten to twenty days after the wounding; all the wounds had received therapy with sulfonamide drugs until that time. In 2 cases bronze wire was used and in 5, a metal plate, with screws. When possible the incision was through normal skin, but in several cases it had to be made through the wound. Penicillin was administered in doses of 600,000 to 700,000 units by the intramuscular route, by perfusion and by injection *in situ*. Results were excellent, with little or no postoperative reaction.

#### INFECTED BONE DEFECTS

Despite the opinion of other authors that bone grafting in the presence of infection usually is unsound, during a period of fourteen months Coleman and others<sup>1076</sup> operated on 52 patients having large bone defects in which infection was present, with only 4 failures. Two of the successes were in cases of abscess of bone due to blood-borne osteomyelitis, which had occurred during childhood. Penicillin therapy was commenced two days before operation and continued after operation from two to five days after the temperature remained normal. Twelve different organisms were obtained from the sites of bone defects, but the same procedure was instituted regardless of their known susceptibility or resistance to penicillin or to the sulfonamide drugs. Cancellous bone chips obtained from the ilium were mixed with penicillin and sulfathiazole and packed into the bone defects after complete excision of all infected scar tissue or granulation tissue, dead bone and previously inserted foreign bodies. In 30 instances, excessive scarring and sinus formation necessitated some sort of plastic closure of the wounds. Closure without drainage or undue tension and the elimination of all dead space, using a full thickness skin graft if necessary to cover the skin defects, were considered essential. Immobilization in a plaster cast, which was not changed for at least three weeks, aided in the healing of soft tissues, and was con-

1075. Arnulf, G.; Ferrand, and Boquet: De l'emploi de la pénicilline dans les ostéosyntheses pour fracture ouverte des membres, Réunions méd.-chir. 1<sup>re</sup> armée franç., pp. 123-129 (Nov. 4) 1944; *ibid.* (Feb. 25) 1945.

1076. Coleman, H. M.; Bateman, J. E.; Dale, G. M., and Starr, D. E.: Cancellous Bone Grafts for Infected Bone Defects: Single Stage Procedure, Surg., Gynec. & Obst. **83**:392-398 (Sept.) 1946.

tinued until the bone was consolidated. In 33 cases, the wounds were perfectly healed at the first change of plaster. The site and causative agent of the bone defects and the type of organism present are listed. The procedure was successful in 92 per cent of the authors' cases.

#### OSTEOMYELITIS

McClintock<sup>1077</sup> describes in detail the indications, measures and means which have been found successful in the treatment of exogenous osteomyelitis by saucerization and early split-skin grafting in several hospitals during the recent war. An illustrative roentgenogram and a photograph of a patient whose case was reported in a previous communication are included.

#### LESIONS OF THE UPPER EXTREMITY

Since the methods employed, the time required and the results obtained in the treatment of lesions of the upper extremity are so different from those in the treatment of lesions of the lower extremity, they should be given separate consideration. Such consideration has been given in 35 cases of lesions of the upper extremity, selected by d' Aubigne and others<sup>1078</sup> from 60 cases of war wounds in which there was loss of bone substance. One hundred thousand units of penicillin per day were given for two days before operation and continued after operation for three days after the patient's temperature became normal. It was considered indispensable for at least one month to have elapsed after complete closure of the soft tissues before any intervention on bone. Notwithstanding all the authors' rigid precautions, an infection with acute suppuration and extrusion of the graft developed five months after intervention. When strength of the graft was desired, cortical bone from the tibia was employed; otherwise, cancellous bone from the iliac crest or the upper portion of the tibia was utilized. The former were usually indicated in defects of the forearm. The fundamental essential for a successful outcome was considered to be pliable overlying soft structures, even though the condition necessitated excision of scar tissue, and a pedicle graft to fill in the defect. The use of osseous material favorable to rehabilitation, careful attention to the circulation and rigid fixation of the fragments are paramount in the treatment.

Uniformly curved and laterally displaced fragments of a soldier's right radius, which had been shattered by a machine gun bullet, persisted

1077. McClintock, J. A.: *Reconstructive Surgery Following Treatment of Osteomyelitis by Saucerization and Early Skin Grafting*, J. Indiana M. A. **39**: 436-439 (Sept.) 1946.

1078. Merle d'Aubigne, R.; Lance, P., and Zimmer, M.: *Traitement des pseudarthroses diaphysaires*, Semaine d. hôp. Paris **22**:1644-1652 (Sept. 21) 1946.

when the usual methods of reduction were attempted by Zaglio and Harris.<sup>1079</sup> Roentgenograms made eleven weeks after the injury showed no essential change in the fragments of bone when compared with those made twenty-four hours after the injury. There was limited flexion of the index finger and complete loss of pronation and supination of the forearm, necessitating surgical removal of displaced bone fragments and bridging of the defect with a tibial graft. At operation, approximately sixteen weeks after the injury, a false aneurysmal sac (or organizing hematoma) was observed to be separating the ulna and the displaced fragments. The postoperative course was uneventful; roentgenograms made four months after the operation showed clinical union of the graft. Six months after the operation, supination was complete, and pronation was 60 per cent of normal. The authors state that uniform deformity of a comminuted bone, observed soon after injury and persisting after the usual ordinary attempts at reduction, is cause for suspecting the presence of a false aneurysm.

Ghinst<sup>1080</sup> reports 4 cases in which the classic signs and symptoms of a syndrome of the sympathetic nervous system persisted after a fracture of the distal end of the radius had healed. All patients were relieved by injection of the sympathetic ganglions with procaine hydrochloride U. S. P. (novocain®). The injections were made twice each week over periods of two to four weeks. In 2 cases, the treatment was commenced five and eighteen months, respectively, after the injury. In the other 2 cases, treatment was commenced six weeks after the injury.

Fernandes Vocos<sup>1081</sup> describes how a combination of osteotomy, by the cubital route of approach, at the site of malunion of the distal end of the radius, and resection of the distal end of the ulna, to correct dysfunction, resulted in the restoration of supination and pronation and in otherwise improved function in the hand and wrist.

During World War II, unfavorable results of bone grafting operations for nonunion of the carpal navicular bone were reported by a number of authors. Murray,<sup>1082</sup> therefore, thought it advisable to report his results in 100 such cases: He experienced excellent results, with good function of the wrist, in the vast majority of cases.

The author states the opinion that certain principles must be followed to obtain the best results. Those he considers most important are con-

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1079. Zaglio, E. R., and Harris, M. H.: Deformity of Radius Produced by Aneurysm: Report of Case, *J. Bone & Joint Surg.* **28**:635-638 (July) 1946.

1080. Ghinst, van der M.: Sur les séquelles des fracture de l'extrémité inférieure du radius et leur traitement, *Bruxelles-méd.* **26**:603-613 (June 9) 1946. 613 (June 9) 1946.

1081. Fernandes Vocos, A.: Fracture mal consolidada de la muñeca: su abordaje por vía cubital, *Bol. y trab., Soc. de cir. de Córdoba* **7**:250-264, 1946.

1082. Murray, G.: End Results of Bone-Grafting for Non-Union., *J. Bone & Joint Surg.* **28**:749-756 (Oct.) 1946.

cisely set forth. The proper selection of patients is emphasized. A few contraindications to the procedure are included. The time relations and the physical findings, as well as a summation of the functional outcome in the entire 100 cases, are listed in a single table. Roentgenograms from 4 cases illustrate the preoperative and postoperative conditions of the fracture site.

A method and technic for arthrodesis of the carpal navicular and capitate bone for nonunion of fractures of the navicular bone are given by Sutro.<sup>1083</sup> In the 4 cases in which the procedure was carried out, all patients had some loss of motion; in 1 case, bony healing was still lacking eight months after operation and nonunion, four years after.

Bone grafting in fracture of the carpal navicular bone by placing three bone pegs across the line of fracture is described by Cobey and White.<sup>1084</sup> Details of the method and clinical data, including case histories, are recorded.

Fontaine and Eck report<sup>1085</sup> 2 cases of fracture of the base of the first metacarpal joint, 1 of the Bennett type and 1 of the Rolando variety. In both instances, the fracture resulted from a bicycle accident. Lambotte screws were used to fix the fragments in position after open reduction. In each case, subluxation had recurred after removal of the plaster, which had been done after attempts at reduction and fixation in hyperextension, as advocated by Boehler. The Bennett type of fracture occurred in the case of a boy of 17, who presented the typical deformity and subjective symptoms so characteristic of this type of fracture. Three months after the accident, the fracture was reduced through an incision in the tabatière anatomique, exposing the fractured fragments. The fragments were fixed in position with Lambotte screws. Fixation in hyperextension until union was firm terminated in a satisfactory anatomic and functional result.

The Rolando variety of fracture occurred in the case of a carpenter of 35. There had been acute pain and total absence of function immediately after the injury. Roentgenograms showed a typical fracture at the base of the thumb, with subluxation of the Rolando type. A local anesthetic was administered, the fracture reduced, and a plaster of paris cast to hold the thumb in hyperextension applied. Twenty days later, roentgenograms and physical examination revealed that the subluxation had recurred and that function was greatly impaired. The fracture was

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1083. Sutro, C. J.: Treatment of Nonunion of Carpal Navicular Bone, *Surg.* **20**:536-540 (Oct.) 1946.

1084. Cobey, M. C., and White, R. K.: Operation for Nonunion of Fractures of Carpal Navicular, *J. Bone & Joint Surg.* **28**:757-764 (Oct.) 1946.

1085. Fontaine, R., and Eck, F.: Screwing as Treatment of Choice in Trapezoid-metacarpal Subluxations Complicating Fractures of Thumb of Bennett or Rolando Type, *Rev. d'orthop.* **32**:76-80 (Jan.-April) 1946.

reduced through an incision in the tabatière anatomique and fixed in position with one small Lambotte screw. Twenty-eight days later, physical and roentgenologic examination revealed an excellent result. Eight months after the intervention, the function was normal. The authors list statistics given by Imbert and Cottalorda on permanent partial disability: In Bennett's fracture, such disability occurred in 5 to 10 per cent of cases and in Rolando's fracture, in 20 to 30 per cent.

The tenon and mortise type of tibial graft was applied by Morris<sup>1086</sup> to bridge metacarpal defects due to gunshot wounds in 6 cases. The grafts all united satisfactorily, and there were no complications. Tibial cortex is used because it is considerably stronger and more suitable for shaping to replace lost segments. The tibial graft is made sufficiently long to bridge the gap and to allow a tenon 1.5 cm. long on both ends. One tenon is fashioned to fit snugly into the medullary cavity of the proximal fragment, and the distal tenon is inlaid in a slot made on the dorsal aspect of the distal fragment, where it is fixed in position with number 31 stainless steel wire.

#### INJURIES TO THE JAW

The use of bone grafts for the remedy of defects of the mandible is a by-product of the first world war. Prior to 1916, only occasional isolated attempts at mandibular grafts were reported. From available figures, approximately 1,000 mandibular bone grafts were reported by workers in all countries from 1916 to 1922.

Between the two wars, defects of the mandible requiring bone grafts were limited to sporadic instances here and there. Owing to prompt and routine application of new methods and materials during World War II large numbers of patients with extensive injuries to the lower part of the face survived.

Blocker and Weiss<sup>1087</sup> report 43 cases in which cancellous bone grafts were successfully taken from the ilium to bridge defects of the mandible, from 3 to 12 cm. in length, and 9 cases in which defects of the maxilla were remedied. The 52 cases were selected from 457 cases of defects of the upper or lower jaws.

It is emphasized that the treatment of bony defects of the jaws must be planned on a basis of long time preparation for the grafting. Elimination of infection, removal of sequestrums and broken fragments of teeth and the remedying of soft tissue defects before surgery is attempted are essentials. The article includes a brief history of mandibular graft-

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1086. Morris, H. D.: Metacarpus-Tenon and Mortise Grafts for Bridging Defects Due to Gunshot Wounds, *Surgery* **20**:364-372 (Sept.) 1946.

1087. Blocker, T. G. Jr., and Weiss, L. R.: Use of Cancellous Bone in Repair of Defects About Jaws, *Tr. South. S. A.* (1945) **57**:153-169, 1946.

ing and the detailed accounting of the types of bone used, plans of treatment, methods of fixation, operative technic and postoperative care; reports on cases follow.

Administration of testosterone propionate for the purpose of encouraging callus formation in a case of fracture of the mandible in a football player is reported by Schmid.<sup>1088</sup> There was no evidence of callus formation after forty-seven days, and roentgenograms showed that the fragments were pulling apart. According to the advice of European authors who had successfully used androgen therapy in the treatment of fractures when callus formation failed to occur in response to the usual methods, three "linguettes," totaling 5 mg., were administered per day for fourteen days. Roentgenographic examination then showed distinct callus formation, and the patient stated that the jaw felt more firm and that he was able to eat harder foods. [ED. NOTE.—The failure of callus to appear in a case of fractured mandible in forty-seven days is not unusual.]

#### PSEUDARTHROSIS OF THE CLAVICLE

Støren<sup>1089</sup> reports a case of pseudarthrosis following fracture of the left clavicle in a woman of 39. The condition had existed for twenty-six years without subjective symptoms. Three years prior to the first examination by the author, severe pain developed in connection with the patient's lifting another woman. For some time, the pain came on only when she was at work and persisted for a short period after work had ceased. Later the pain, characterized as intolerable, became persistent and was not influenced by various physical therapy measures. The pain was repeatedly localized to sharply defined areas on the back of the upper arm and the forearm. Subcutaneous vasomotor changes, consisting of tenderness, hyperemia and induration, were present in the two areas.

Roentgenograms revealed a pseudarthrosis at the junction of the middle and outer thirds of the clavicle, with considerable upward angulation of the fragments. An attempt to produce osteosynthesis by drilling and by fixation with wire sutures relieved the pain for only four weeks, union failing to occur. A second operation, which consisted of placing a tibial graft with two "bridgeheads" across the clavicular defect, was then performed. The graft was fixed in position with a metal suture. Bony union, accompanied by the disappearance of all the objective and subjective symptoms, followed.

1088. Schmid, H.: Favorable Effect of Testosterone Propionate (Androgen) on Callus Formation in Case, *Schweiz. med. Wchnschr.* **76**:538 (June 15) 1946.

1089. Støren, H.: Old Clavicular Pseudarthrosis with Late Appearing Neuralgias and Vasomotor Disturbances Cured by Operation, *Acta chir. Scandinav.* **94**:187-191, 1946.

Figure drawings to show the areas of localized pain with vasomotor changes, one diagrammatic drawing of the "bridgehead" graft employed, and preoperative and postoperative roentgenograms illustrate the presentation.

[ED. NOTE.—In dealing with pseudarthrosis of the clavicle, it should always be remembered that congenital defects of this bone are one of its prime characteristics. Such defects may vary in degree from those which are slight, amounting to a false joint, to those in which most of the bone, as well as part of the sternum, may fail to develop, as seen in congenital craniocleidodysostosis. Congenital defects of the clavicle are commonly bilateral. Their explanation is probably that the sternal end of the clavicle is formed in membrane, while the outer end is enchondral bone.]

#### POST-TRAUMATIC CONTRACTURES

Using the Sherrington pattern of "decerebrate rigidity" on cats whose brains were separated in the region of the tentorium Speranski<sup>1090</sup> employed various methods of producing irritation in the extremities in an attempt to explain post-traumatic contractures. Both central and peripheral irritation were investigated. Prolonged observation revealed intermittent relaxation of the spasticity, not only in the affected limb but also in the homolateral one. The author concludes that this phenomenon can be explained only by the fact that the irritation spreading through the nervous system is of a reciprocal character, involving the neural segments.

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1090. Speranski, A. D.; Post-Traumatic Contractures, *Am. Rev. Soviet Med.* 4:22-24 (Oct.) 1946.

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#### CORRECTION

In the article by Henry Milch, M.D., on the "Short Radius" in the October issue of the *ARCHIVES*, page 856, the quotation from Anton, Reitz and Spiegel should read "idiopathic, progressive curvature of the radius due to a dyschondroplasia of the inferior radial epiphysis resulting in a deformity of the wrist giving the appearance of an anterior (or more rarely a posterior) subluxation of the hand."

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